Systemic Therapy Update

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Inside This Issue:

EDITOR'S CHOICE

NEW DRUG PROGRAMS

Gastrointestinal:

The **Provincial Systemic Therapy Program** has approved **capecitabine** and **oxaliplatin** as combination therapy for the adjuvant treatment of high-risk stage IIB and stage III colon cancer **(UGIAJCAPOX)**. UGIAJCAPOX is an alternative treatment option to FOLFOX (UGIAJFFOX). This is based on data from a phase III trial involving 1886 patients with stage III colon cancer. Adjuvant capecitabine/oxaliplatin significantly improved the 5-year disease free survival (DFS) compared to fluorouracil/leucovorin alone (66.2% vs. 59.8%, HR 0.80, 95% CI 0.69-0.93), and showed a trend towards improved 5-year overall survival (OS) (77.6% vs. 74.2%, HR 0.87, 95% CI 0.72-1.05). [Haller *et al. J Clin Oncol* 2011;29(11):1465] Although cross-comparison across trials should be done with caution, the overall survival associated with FOLFOX in the MOSAIC trial was comparable with that of capecitabine/ oxaliplatin (FOLFOX 6-yr OS 72.9% vs. CAPOX 5-yr OS 77.6%). [André *et al. NEJM* 2004;350(23):2343.]

Neuro-Oncology:

The **Provincial Systemic Therapy Program** has approved the addition of **temozolomide in metronomic dosing** (continuous dose-intense, 50 mg/m^2 daily) to the Benefit List for the treatment

EDITOR'S CHOICE

of relapsed malignant gliomas **(UCNTEMOZMD).** Preclinical studies suggest that daily 50 mg/m^2 dosing of temozolomide may overcome drug resistance by depleting the cellular levels of O^6-methylguanine DNA methyltransferase (MGMT) repair enzymes. In a phase II study involving 120 patients with glioblastoma multiforme (GBM) who were previously treated with standard dose of concomitant and adjuvant temozolomide (CNAJTZRT), the 6-month progression-free survival (PFS) was 27-36%. These results were superior to those seen in a trial evaluating standard temozolomide dosing in relapsed GBM (21%) or traditional procarbazine therapy (8%). [Perry *et al. JCO* 2010;28(12):2051-7]

MEDICATION SAFETY UPDATE

VENOUS THROMBOEMBOLISM PROPHYLAXIS FOR HOSPITALIZED CANCER PATIENTS

Venous thromboembolism (VTE) occurs in up to 20% of patients with cancer and is one of the leading causes of death in this patient population.[1] The actual rate of VTE is suspected to be underestimated and has been reported in up to 50% of cancer patients at the time of post-mortem examination.[2] There are various levels of risk among cancer patients and the rate of VTE can differ substantially depending on patient characteristics.[1,3] For example, risk varies with age, obesity, comorbidities, immobilization and the presence of metastatic disease. The level of risk is also dependent on the primary site of the cancer.[1,3] Although it is evident that cancer patients carry a high inherent risk for VTE and that VTE can significantly impact morbidity and mortality, studies show that many cancer patients do not receive appropriate thromboprophylaxis therapy in the inpatient setting.[4]

A new BCCA Vancouver Centre Policy and Pre-Printed Order (PPO) have recently been implemented to standardize the risk assessment for VTE and the indication for prophylactic therapy among admitted patients. This initiative aligns with the new requirements of Accreditation Canada and ensures that admitted cancer patients are routinely assessed for VTE prophylactic therapy to help reduce the risk of this highly preventable complication.

According to the new policy, all inpatients (with the exception of short-stay patients) are deemed "high risk" on the basis of their cancer diagnosis. This is in accordance with the definition of "high risk" in the 2007 American Society of Clinical Oncology VTE guidelines.[5] All patients are considered eligible to receive VTE prophylaxis unless they meet any of 3 criteria: (1) expected length of stay less than 24 hours, (2) currently receiving anticoagulation therapy at treatment doses, or (3) contraindication to anticoagulation therapy (i.e. high risk for serious bleeding into a critical site). The PPO prompts the prescriber to choose VTE prophylactic therapy, or to indicate why the patient is not eligible for therapy (select from a list of applicable contraindications). All admitted patients are also given a written education pamphlet on the risk factors and associated signs and symptoms of VTE.

Low molecular weight heparin (LMWH) is the drug of choice for VTE prophylaxis in cancer patients. Dalteparin is chosen as the LMWH of choice at the BCCA because it is cost-effective and requires only once daily dosing. Unfractionated heparin is preferred for patients with a creatinine clearance of less than 10 mL/min.

Medication Safety Update

References:

1. Ay C, Dunkler D, Marosi C, *et al.* Prediction of venous thromboembolism in cancer patients. *Blood* 2010; 116(24): 5377.
2. Lyman GH. Venous thromboembolism in the patient with cancer. *Cancer* 2011; 117(7):1334.
3. Khorana AA, Connolly GC. Assessing risk of venous thromboembolism in the patient with cancer. *J Clin Oncol* 2009;27(29):4839.
4. Petersen LJ. Anticoagulation therapy for prevention and treatment of venous thromboembolic events in cancer patients: a review of current guidelines. *Cancer Treat Rev* 2009;35(8):754.
5. Lyman GH, Khorana AA, Falanga A, *et al.* American Society of Clinical Oncology Guideline: Recommendations for Venous Thromboembolism Prophylaxis and Treatment in Patients with Cancer. *J Clin Oncol* 2007;25:5490.

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Drug Update

Abiraterone Access Progarm

Abiraterone (ZYTIGA®), an orally administered androgen biosynthesis inhibitor, has been approved by Health Canada, in combination with prednisone, in patients with metastatic, castration-resistant prostate cancer (mCRPC) previously treated with DOCEtaxel. BC Cancer Agency funding for abiraterone is currently under review. Patients who had previously received abiraterone through the Health Canada Special Access Programme (SAP) may now obtain the drug through the manufacturer's (Janssen Canada) drug access program, ZAP. Completion of a program enrollment form is required for patients newly initiated on abiraterone.

BCCA pharmacies have agreed to dispense and counsel patients on abiraterone. CON pharmacies may contact McKesson Specialty (supplier) at 1-855-998-4423 or zytiga@supportprogram.com to determine if they can support this service. For more information on abiraterone access, please see the Patient Assistance Programs website at http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms.htm.

Cancer Drug Manual

New Monograph

Pazopanib Monograph, Patient Handout and Hazardous Drug Evaluation have been completed. Expert review was provided by Dr. Christian Kollmannsberger (GU Systemic Therapy Group Chair) and Victoria Kletas (GU Tumour Group Pharmacist). Pazopanib is available through the BCCA Compassionate Access Program (CAP) for metastatic renal cell carcinoma at a recommended dose of 800 mg orally once daily.

- Special precautions should be considered in patients with cardiac dysfunction, including

hypertension, decreased left ventricular ejection fraction (LVEF) and QT-prolongation. Pazopanib has been associated with less than 1 % incidence of hypertensive crisis, significant reduction in LVEF which may be asymptomatic, and less than 1 % incidence of Torsades de Pointes.

- Elevations in serum transaminases and bilirubin may occur, the latter being of more significant concern.
- Main side effects include hypertension, diarrhea, hair de-pigmentation, nausea, vomiting and anorexia. Hypertension commonly occurs within the first 18 weeks of treatment and may be managed with antihypertensives. The gastrointestinal side effects are mild and can be managed with prophylactic antiemetics using Low-Emetogenic Potential regimens.

REVISED MONOGRAPHS

Bicalutamide Monograph has been revised to update the Interactions section to include more details about cytochrome P450 interactions. The Side Effects table has been revised according to the current template standard.

CISplatin Handouts have been revised to add TALLman lettering and to update all template statements, including the names of all supportive care documents, in the Side Effects table.

Cyclophosphamide Monograph has been revised to update the management of hydrochlorothiazide interactions in the Interactions table.

Dasatinib Monograph has been revised to add a new caution about pulmonary arterial hypertension in the Caution section and a new side effect paragraph after the Side Effects table.

DOXOrubicin Handouts have been revised to add TALLman lettering and to update all template statements, including the names of all supportive care documents, in the Side Effects table.

Octreotide Monograph has been revised to add cardiovascular side effects to the Side Effects table and a new caution about bradycardia, arrhythmias and conduction abnormalities to the Caution section. The Supply and Storage section has been completely updated, and the Side Effects table and Solution Preparation and Compatibility section have been revised according to the current template standard.

Panitumumab Monograph has been revised according to the current template standard.

SUNItinib Monograph has been revised to add a new caution about osteonecrosis of the jaw (ONJ) in the Caution section. Dosing information has also been updated for renal failure, hepatic failure, and dialysis in the Dosing section.

BENEFIT DRUG LIST

NEW PROGRAMS

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

- **Capecitabine** and **Oxaliplatin** (case-by-case) for adjuvant treatment of stages IIB and III colon carcinoma (UGIAJCAPOX)
- **Temozolomide Metronomic Dosing** (case-by-case) for relapsed malignant gliomas (UCNTEMOZMD) after completion of standard-dose concomitant/adjuvant temozolomide (CNAJTZRT)

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
UGIAJCAPOX	☑	☑	☐	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer Using Oxaliplatin and Capecitabine

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UCNBEV	☑	☐	☐	*Updated Exclusions section*	Palliative Therapy for Recurrent Malignant Gliomas Using Bevacizumab
UCNTEMOZMD	☑	☐	☐	*Revised Eligibility section*	Therapy for Malignant Brain Tumours Using Metronomic Dosing of Temozolomide
GICART	☑	☐	☐	*Minor typo corrected in Treatment section*	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Mitomycin, Capecitabine and Radiation Therapy

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
LYCHOPR	☑	☐	☐	*Serum bilirubin clarified in Tests section*	Treatment of Lymphoma with DOXOrubicin, Cyclophosphamide, Vincristine, Prednisone and Rituximab (CHOP-R)

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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Oncology Drug Information	604.877.6275		druginfo@bccancer.bc.ca
Education Resource Nurse	604.877.6000 x 2638		nursinged@bccancer.bc.ca
Library/Cancer Information	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 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
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 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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