Systemic Therapy Update

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INSIDE THIS ISSUE

EDITOR'S CHOICE

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

The **Sarcoma Tumour Group** has revised the eligibility of **Imatinib** in the SAAVGI protocol to include patients with ***c-KIT negative*** gastrointestinal stromal tumour (GIST). Imatinib is effective in most cases of c-KIT positive GIST and in some cases of GIST with PDFGRA mutations. However, case series suggest that c-KIT negative patients may also respond to imatinib (*Blackstein et al. ASCO 2005 abstr 9010*). Therefore, a therapeutic trial of imatinib is worthwhile in all patients with GIST irrespective of the c-KIT status given the high probability of eliciting a response. Of note, based on the 5-year referral data at BCCA, only 3 out of 156 patients with GIST were not c-KIT positive. Of these three patients, one was PDFGRA+, one wild type, and one of unknown status.

The BCCA Guidelines on Chemotherapy-Induced Nausea and Vomiting (SCNAUSEA) have removed **Dolasetron** as an option for the 5-HT3 antagonists. Recent data showed that dolasetron can increase QT intervals and therefore the potential risk of developing fatal torsade de pointes. In a randomized study recommended by the US Food and Drug Administration, dolasetron was compared to placebo and an active control involving 80 healthy adults. Dolasetron was compared to placebo and active control in 80 healthy adults. Dolasetron was associated with a dose-dependent increase in QT interval to 14.1 ms for the 100 mg (therapeutic) and 36.6 ms for 300 mg (supratherapeutic) doses. Drugs that prolong QT interval beyond 20 ms are usually considered to pose a significant risk of promoting arrhythmia.

MEDICATION SAFETY – TALLMAN LETTERING AT BCCA

Many drug names are recognized to cause confusion and errors because they are similar in appearance or sound.[1] These are known as Look-Alike/Sound-Alike drugs. Reports suggest that up to 25% of medication errors are due to medication names that look or sound alike.[2] In oncology, mix-ups between medications are even more concerning due to their high rate of toxicity, which could potentially result in catastrophic consequences. For example, mix-ups have occurred between:

- CISplatin and CARBOplatin
- DOCEtaxel and PACLitaxel
- vinCRIStine and vinBLAStine

Confirmation bias is considered to play a role in the cause of medication mix-ups.[3] Confirmation bias occurs when a healthcare provider reads the name of a medication and "sees" what they expect to see, rather than what they truly see. This happens because the brain only selectively notices or focuses on what is familiar to them and not on what is actually there. In fact, it "*deosn't mttaer how wrods are rwitten bcuseae the huamn mind deos not raed evrey ltter*". It is human nature to associate with familiarity, but it is important to recognize how confirmation bias plays a role in medication errors and how they can be prevented.[4]

TALLman lettering is a risk reduction strategy that reduces errors by printing sections of the drug name in capital letters to emphasize differences between Look-Alike/Sound-Alike drugs. TALLman lettering is recommended by the Institute for Safe Medication Practices (ISMP) for incorporation into all forms of drug communication. As such, it has become a widely accepted method for distinguishing similar drug names in the healthcare setting in order to avoid unintended interchange of Look-Alike/Sound-Alike drugs.

A new BCCA pharmacy directive has been approved to integrate TALLman lettering in BCCA databases and materials to help prevent medication mix-ups. Incorporation into documents and databases will be gradual, and will require resources to determine IT capabilities of various systems. In the near future, TALLman lettering will also be adopted by the Systemic Therapy Program and will encourage TALLman lettering to be used in memos, alerts, policies, and other forms of communication throughout the Agency on an ongoing basis.

References:

1. ISMP Canada Safety Bulletin, November 11, 2010, Volume 10, Number 8: page 1-4. http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2010-08-TALLmanforOncology.pdf
2. Filik R, Price J, Darker I, et al. The influence of tall man lettering on drug name confusion. *Drug Saf* 2010; 33(8):677.
3. Schulmeister L. Look-Alike, sound-alike oncology medications. *Clin J Oncol Nur* 2006; 0(1):35.
4. ISMP Frequently Asked Questions, Accessed Feb 18, 2011. http://www.ismp.org/faq.asp#Question_9

DRUG UPDATE – THYROTROPIN-ALFA SHORTAGE

Shortage of Thyrotropin-alfa (THYROGEN®) is expected to last until sometime in June 2011. This is due to a disruption in supply from the manufacturing facility and Genzyme, the manufacturer, currently has no more stock. There is no adequate therapeutic substitutes or alternate supplier of this product. Therefore, prescribers and pharmacies will need to collaborate to develop a process to allocate the stock for the patients already booked for treatment.

COMMUNITIES ONCOLOGY NETWORK – REMINDER ABOUT OSCAR SUBMISSION DEADLINE

The 2010/11 fiscal year will end on **Thursday 31 March 2011**. This brings with it tight deadlines which must be met for external reporting to the Ministry of Health and the Office of the Comptroller General. All claims for this fiscal year must be invoiced by 11:59 pm **Sunday 10 April 2011** via OSCAR (Online System for Cancer Drugs Adjudication and Reimbursement). Any claims invoiced after that date will not be eligible for reimbursement. For more information, please contact oscar@bccancer.bc.ca.

CANCER DRUG MANUAL

Iniparib Interim Monograph has been developed. Iniparib causes DNA damage and cell death via PARP1 inhibition. Iniparib is only available via the Heath Canada' Special Access Programme for the treatment of breast cancer and requires BCCA Compassionate Access Program (CAP) approval. A dose of 5.6 mg/kg IV is given on days 1, 4, 8, and 11 as part of a 21-day cycle. Highlights from this document:

- Drug interactions should be considered during treatment. Drugs known to deplete glutathione concentrations (e.g., acetaminophen) may increase iniparib levels and consequently, its effects. Iniparib may also alter the metabolism of drugs metabolized by CYP 1A2.
- Phototoxicity has been observed *in vitro*. Direct sunlight should be avoided and use of a suitable sunscreen is suggested.
- The most frequent adverse effects appear to include nausea, fatigue, constipation, anemia and neutropenia. CNS toxicity, including convulsions, has been observed at higher dosage levels in animal toxicology studies and is considered as a possible risk with treatment.

Iniparib has also been added to the **Chemotherapy Preparation and Stability Chart.**

Denosumab Interim Monograph has been developed. Denosumab is a human monoclonal antibody that inhibits human RANK ligand, thus preventing osteoclast-mediated bone destruction. It has been used in the treatment of giant-cell tumour of the bone. BCCA CAP approval is required for this indication. Denosumab is available as a 60 mg (1 mL) prefilled syringe. Usual dose in giant-cell tumour is 120 mg SC given on days 1, 8, and 15 of month 1, followed by a 120 mg SC dose on day 1 of month 2, and a 28-day cycle thereafter. Highlights from this document:

- Frequently reported adverse events include: extremity pain, back pain, and headache.
- Osteonecrosis of the jaw has been reported (1.1%).
- Hypocalcemia and disorders affecting mineral metabolism must be corrected prior to treatment. Adequate intake of calcium and vitamin D during treatment is important.
- The cap of the prefilled syringe contains latex.

Capecitabine Monograph has been revised to update the role of pyridoxine in hand/foot syndrome in the paragraph below the Side Effects table. Pyridoxine is no longer considered effective in the prevention of hand/foot syndrome. **Capecitabine Patient Handout** has been revised to delete the pyridoxine recommendation from the Side Effect table. For more information, see the January issue of the Systemic Therapy Update (www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate).

Fluorouracil Monograph has been revised to delete the recommendation to use pyridoxine for the prevention of hand/foot syndrome. Pyridoxine is no longer considered effective for this purpose.

Tamoxifen Patient Handout has been revised to update cholesterol and triglycerides information in the Side Effects table.

The Cancer Drug Manual Team would like to welcome

- **Dr. Greg Dueck** to the Editorial Board as a physician representative. Dr. Dueck is an oncologist with BCCA – Centre for the Southern Interior (Kelowna). His primary interest is lymphoma/myeloma, but he also treats melanoma and CNS tumours.
- **Karen Mason** to the CDM writing team. Karen is a staff pharmacist at BCCA – Fraser Valley Centre.

The Cancer Drug Manual Team would like to bid farewell to CDM Editorial Board member, Marney McKay as she steps down 1 March 2011. The team would like to thank Marney for all her contributions during her time on the board.

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
UBRAJACTW	☑	☑	☐	Adjuvant Therapy for Early Breast Cancer Using Doxorubicin and Cyclophosphamide Followed By Weekly Paclitaxel
UBRAJFECDT	☑	☑	☐	Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide Followed By Docetaxel and Trastuzumab
UGUAJPG	☐	☐	☑	Adjuvant Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine
GUNAJPG	☐	☐	☑	Neo-Adjuvant Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine
SMTAM	☐	☐	☑	Therapy for Malignant Melanoma Using Tamoxifen

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVPAM	☐	☑	☐	*Tests clarified*	Treatment of Acute Bone Pain Secondary To Breast Cancer Metastases Using Pamidronate.
BRAVT7	☑	☑	☐	*Requirement for CAP approval removed, protocol code and eligibility revised*	Palliative Therapy for Metastatic Breast Cancer Using Weekly Paclitaxel

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UGIAJFFOX	☑	☑	☐	*ANC threshold revised*	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin)
GIAVPG	☑	☐	☐	*Renal dosing clarified*	First-Line Palliative Chemotherapy for Advanced Gallbladder Cancer and Cholangiocarcinoma Using Gemcitabine and Cisplatin
UGIAVCETIR	☑	☑	☐	*Management of hypomagnesemia revised*	Third Line Treatment of Metastatic Colorectal Cancer Using Cetuximab in Combination with Irinotecan
UGIAVPANI	☑	☑	☐	*Management of hypomagnesemia revised*	Palliative Third Line Treatment of Metastatic Colorectal Cancer Using Panitumumab
UGICAPOX	☑	☑	☐	*ANC threshold revised*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, and Capecitabine
UGICOXB	☑	☑	☐	*ANC threshold revised*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, Bevacizumab and Capecitabine
UGIFFIRB	☑	☑	☐	*Timing of protein urinalysis clarified*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Irinotecan, Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab
UGIFFOXB	☑	☑	☐	*ANC threshold revised, timing of protein urinalysis clarified*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, 5-Fluorouracil, Folinic Acid (Leucovorin) and Bevacizumab
UGIFOLFOX	☑	☑	☐	*ANC threshold revised*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin)
UGIRAJFFOX	☑	☑	☐	*ANC threshold revised*	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer Using Oxaliplatin, 5-Fluorouracil and Folinic Acid (Leucovorin)
GUAVPG	☑	☑	☐	*Antiemetics and renal dosing clarified, diluent volume*	Palliative Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine
GUBEP	☑	☑	☐	*Aprepitant dosing clarified, treatment table reformatted*	Curative Therapy for Germ Cell Cancer Using With Bleomycin, Etoposide, Cisplatin for Germ Cell Cancers
UGUEVER	☑	☐	☐	*Dose modifications clarified*	Therapy for Advanced Renal Cancer Using Everolimus
HNLAALTPRT	☐	☐	☑	*Treatment cycles clarified*	Treatment for Advanced Head and Neck Cancer Using Cisplatin During Radiation Therapy
UHNLACETRT	☐	☑	☐	*Return appointments clarified*	Combined Cetuximab and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UHNLADCF	☑	☐	☐	*Aprepitant dosing clarified, new reference added*	Treatment of Locally Advanced Squamous Cell Carcinoma of the Head and Neck with Docetaxel, Cisplatin and Infusional Fluorouracil
HNLAPRT	☑	☐	☐	*ANC clarified in Dose Modifications*	Combined Chemotherapy (Cisplatin) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
HNNLAPG	☑	☐	☐	*Hepatitis B information added*	Induction Treatment of Locally Advanced Nasopharyngeal Cancer With Cisplatin and Gemcitabine
HNNLAPRT	☑	☑	☐	*Hepatitis B information added, blood work clarified*	Treatment of Locally Advanced Nasopharyngeal Cancer With Concurrent Cisplatin and Radiation
ULKMDSA	☑	☐	☐	*Eligibility and Tests clarified*	Therapy of Myelodysplastic Syndrome Using Azacitidine
LYCODOXMR	☑	☑	☐	*Rituximab infusion time clarified*	Treatment of Burkitt Lymphoma and Leukemia (ALL-L3) With Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate, Leucovorin (CODOX-M) and Rituximab
LYIVACR	☑	☑	☐	*Rituximab infusion time clarified, non-PVC caution added*	Treatment of Burkitt Lymphoma and Leukemia (ALL-L3) With Ifosfamide, Mesna, Etoposide, Cytarabine (IVAC) and Rituximab
UMYBORPRE	☑	☑	☐	*Tests and Dose Modifications clarified*	Treatment of High Risk Multiple Myeloma Using Bortezomib, Dexamethasone With or Without Cyclophosphamide As Induction Pre-Stem Cell Transplant
UMYBORREL	☑	☑	☐	*Tests and Dose Modifications clarified*	Treatment of Relapsed Multiple Myeloma Using Bortezomib, Dexamethasone With or Without Cyclophosphamide
UMYLENDEX	☐	☑	☐	*Cycle number clarified*	Therapy of Multiple Myeloma Using Lenalidomide With Dexamethasone
UMYMPBOR	☑	☑	☐	*Tests and Dose Modifications clarified*	Treatment of Multiple Myeloma Using Melphalan, Prednisone and Weekly Bortezomib With the Option of Substituting Cyclophosphamide for Melphalan
SAAVGEMD	☑	☐	☐	*Antiemetics and infusion time clarified*	Second or Third Line Therapy for Soft Tissue Sarcomas Using Gemcitabine and Docetaxel
SAAVGI	☑	☑	☐	*Eligibility revised to include c-KIT negative GIST*	Treatment of Advanced c-kit Positive and c-kit Negative Gastrointestinal Stromal Cell Tumors (GIST's) Using Iimatinib
SCNAUSEA	☑	☐	☐	*Dolasetron removed*	Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults

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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