Systemic Therapy Update

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EDITOR'S CHOICE

2011-2012 NEW DRUG PROGRAM

The **Provincial Systemic Therapy Program** has approved **pazopanib** as first-line agent for palliative therapy of renal cell carcinoma (RCC) with a clear cell component **(UGUPAZO)**. Pazopanib will serve as an alternative to SUNItinib, the reference standard, in patients not previously treated with systemic therapy and in those refractory to cytokine therapy (i.e. interferon-alpha).

In a phase III trial, pazopanib was associated with increased progression-free survival (PFS) compared to placebo (9.2 mo vs. 4.2 mo). The magnitude of this benefit is similar to that seen with SUNItinib and SORAfenib in other trials. Pazopanib exhibits a lower incidence of hand foot syndrome, diarrhea, asthenia and myelosuppression. Common adverse effects of pazopanib include GI toxicities, anorexia, hypertension and hair colour changes. An ongoing phase III, open-label trial designed to directly compare the efficacy, safety and tolerability of pazopanib versus SUNItinib in locally advanced and/or metastatic renal cell carcinoma (mRCC) patients will be completed in 2012. This trial will further guide therapy selection between pazopanib and SUNItinib as first-line treatment in patients with advanced RCC.

EDITOR'S CHOICE

Overview of Renal Cell Carcinoma and Current Management:

In British Columbia, the incidence of renal cell carcinoma is 11.7/100,000 in males and 7.4/100,000 in females. There are numerous histologic subtypes with approximately three quarters of tumours being of the clear cell subtype; papillary, chromophobe carcinoma and oncocytoma account for the remainder.

The mainstay of treatment is surgery such as radical nephrectomy with or without regional node dissection for localized disease. Radiation therapy has no established role as primary definitive therapy of early renal cancers or as adjuvant therapy with surgery. It may be used to control bleeding and pain from the primary tumour and to palliate symptoms from metastases. RCC is refractory to cytotoxic chemotherapy but responds well to targeted agents in metastatic disease.

Historically, interferon-alpha (GUKIFN) was used in selected RCC patients with good prognostic factors (clear cell histology, good performance status, progression-free interval following initial diagnosis of more than one year, and preferably lung metastasis as the sole metastatic site), but was associated with significant toxicities. Since the introduction of anti-angiogenic agents, in particular small molecule tyrosine kinase inhibitors against VEGF receptor and mTOR inhibitors, these agents have largely replaced interferon-alpha as the standard of care in RCC with clear cell histology.

The following table provides an overview of the different treatment options available for mRCC patients with clear cell histology:

Indication	Treatment	Administration Guideline
First-line therapy	SUNItinib *(UGUSUNI)*	▪ Orally administered tyrosine kinase inhibitor (TKI) ▪ Reference standard for first-line therapy in mRCC
	Pazopanib *(UGUPAZO)*	▪ Orally administered TKI ▪ First-line treatment alternative to SUNItinib in patients with no prior systemic therapy and as an option for cytokine-refractory patients
	SORAfenib *(UGUSORAF)*	▪ Orally administered TKI ▪ Alternative first-line treatment in patients unsuitable for first-line SUNItinib or pazopanib
	Temsirolimus *(UGUTEM)*	▪ Intravenously administered inhibitor of mammalian target of rapamycin (mTOR) ▪ It should be only considered for patients with mRCC with poor prognostic factors.
Second-line therapy	Everolimus *(UGUEVER)*	▪ Orally administered inhibitor of mTOR ▪ Agent of choice in mRCC after failure of SUNItinib, SORAfenib and/and pazopanib

Ongoing clinical trials examining efficacy, safety and tolerability will provide further guidance in the selection of therapy among different agents available for the treatment of renal cell carcinoma.

References:
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Submitted by:
Victoria Kletas BScPharm, MSc(Pharm)
GU Tumour Group Pharmacist
Oncology Drug Information Specialist
Provincial Systemic Therapy Program

Reviewed by:
Dr. Christian Kollmannsberger MD, FRCPC
GU Systemic Therapy Group Chair
Clinical Associate Professor of Medicine
Div. of Medical Oncology
University of British Columbia

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

Changes in Capecitabine Dosing Schedule in Rectal Carcinoma Chemotherapy Protocol, PPPO and Patient Handout:

The **Gastrointestinal Tumour Group** has revised the **capecitabine** administration standard in the **GIRCRT Protocol, PPPO** and **Patient Handout**. The change involves capecitabine given only on the days that radiation therapy is given**.** The protocol had previously used a 7-day administration schedule. In the recent NSABP R-04 trial, 1,608 patients with stages II and III rectal cancer undergoing RT were randomized to continuous intravenous infusion of 5-FU administered 5 days/week (with or without oxaliplatin) vs. capecitabine administered 5-days/week (with or without oxaliplatin). No significant differences were observed between 5-FU and capecitabine in the rates of pathologic complete response (pCR) (18.8% vs. 22.2%, p=0.12), surgical downstaging (20.7% vs. 23.0%, p=0.62), and the need for sphincter saving surgery (61.2% vs. 62.7%, p=0.59). (Roh *et al. J Clin Oncol* 29: 2011[suppl; abstr 3503]) This emerging evidence and the intent to standardize drug use to optimize patient safety prompted a revision of the GIRCRT protocol, PPPO and patient handout.

Revisions to Trastuzumab-Containing Pre-Printed Orders :

The **Trastuzumab**-containing pre-printed orders are revised to include space to indicate the dosing weight. All affects protocols are listed in Revised Protocols, PPPOs and Patient Handouts table.

EDUCATION UPDATE

BCCA PHARMACY PRACTICE RESIDENCY PROGRAM – JUNE 2012

It is with great pleasure that the **Provincial Systemic Therapy Program** announces the **BC Cancer Agency Pharmacy Practice Residency Program** to commence in June 2012. The Pharmacy Residency Program will be a one-year, BCCA-wide experiential learning program that will focus on developing the following skills in a pharmacy resident: (1) core clinical skills in patient care, (2) inter-professional collaboration, (3) leadership, (4) teaching, and (5) project management. The program will include both clinical and non-clinical rotations such as drug distribution/IV admixture, drug information, practice management, medication safety, inpatient oncology care, ambulatory oncology care, pain and symptom management, and direct patient care rotations in common tumour sites. One residency position will be available in the first year of the program.

This program will be the third Pharmacy Practice Residency Program in Canada to be conducted in an oncology institution. The program will be affiliated with the University of British Columbia and will be seeking accreditation status from the Canadian Hospital Pharmacy Residency Board of Canada (CHPRB). As a centre of excellence in oncology academia and research, the BCCA is committed to providing strong clinical training to health professionals to advance clinical practice and improve patient care. The BCCA Pharmacy Practice Residency Program will provide a unique training opportunity to pharmacists to improve oncology patient care.

More information on the program can be found on the following websites:

- UBC website: http://www.pharmacy.ubc.ca/programs/non-degree-programs/residency/participating-hospitals/bc-cancer-agency
- CSHP Accredited Residency Programs website: http://206.191.51.166/programs/residencyTraining/accreditedPrograms/index_e.asp

Online applications are now open. The deadline for application submission is **October 15, 2011**. Eligible applicants include individuals with a Bachelor of Science Degree in Pharmacy who are eligible for licensure with the College of Pharmacists of BC. To learn more about the application process, please visit:

- CSHP Residency Training Website - http://206.191.51.166/programs/residencyTraining/applicantsinfo_e.asp
- UBC Pharmacy Practice Residency Program Website - http://www.pharmacy.ubc.ca/programs/non-degree-programs/residency/apply%20

For more information about the BCCA Pharmacy Practice Residency Program, please contact the Program Director and Coordinator.

Susan Walisser BScPharm, ACPR
Residency Program Director
SWalisse@bccancer.bc.ca

Sally Man BScH, BScPharm, ACPR, PharmD
Residency Program Coordinator
SMan3@bccancer.bc.ca

DRUG UPDATE

SHORTAGE OF PEGYLATED LIPOSOMAL DOXORUBICIN (CAELYX®)

There is currently a world-wide supply shortage of **pegylated liposomal DOXOrubicin (CAELYX®)**. Inventory is expected to be intermittent over the next few months, and it is unclear when this issue will resolve. The drug shortage is due to production difficulties experienced by Janssen Inc., the manufacturer. DOXIL®, a pegylated liposomal DOXOrubicin product marketed in the United States, is also undergoing a critical supply shortage. Its emergency supply program (DOXIL® C.A.R.E.S. Physician Access Program) will not be accessible to patients outside the US.

The affected chemotherapy protocols include **GOOVLDOX**, **GOOVPLDC** and **KSLDO**. Prescribers and pharmacies are collaborating to develop a process to allocate the stock for patients already booked for treatment. The gynecology tumour group and physicians managing Kaposi's Sarcoma patients have provided a number of recommendations as treatment alternatives. These recommendations are presented in the table below. Please note that the use of chemotherapy protocols outside the pre-specified eligibility criteria will require submission to and approval by the BCCA Compassionate Access Program (CAP). Pharmacy will continue to communicate updates on the supply shortage status to BCCA and CON centres.

Tumour Group	Affected Protocols	Recommended Alternatives
GYNE	GOOVLDOX	a) Treatment break if appropriate. b) Delay treatment if appropriate. c) If treatment continuation is indicated, depending on the prior treatment history and response to prior therapy, 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 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 be directly compared to liposomal DOXOrubicin in a clinical trial setting. It is important to note the different adverse effect profile between liposomal DOXOrubicin and DOXOrubicin, particularly alopecia and cardiotoxicity/contraindication in coronary artery disease.
	GOOVPLDC	d) Treatment break if appropriate. e) Delay treatment if appropriate. f) If treatment continuation is indicated, switch to: a) GOOVCATR or GOOVCAG, or b) Continue single-agent CARBOplatin as per GOOVPLDC until pegylated liposomal DOXOrubicin supply is re-established.

DRUG UPDATE

Kaposi's Sarcoma	KSLDO	▪ Substitute with liposomal DAUNOrubicin 40 mg/m^2 IV. Repeat every 14 days.* ▪ Substitute with KSAD.

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

SHORTAGE OF THYROTROPIN ALFA – AN UPDATE

The drug shortage of **thyrotropin alfa (THYROGEN®)** continues to persist despite previous communication from Genzyme, the manufacturer, that the drug would be available by June 2011. The most recent update from Genzyme indicates that the supply is now completely depleted and that temporary shipment delays and regional disparities in supply availability are expected to continue for the remainder of 2011 and throughout 2012. There are no viable therapeutic substitutions or alternate supplier for this product. Prescribers and pharmacies will continue to collaborate to allocate the stock for patients already booked for treatment.

CANCER DRUG MANUAL

TRANSLATION OF PATIENT INFORMATION

Chinese and Punjabi translations of the Patient Handouts on **capecitabine** and **fluorouracil** are now available on the Cancer Drug Manual website with the corresponding English versions. This is part of a pilot project in translating patient information of selected drugs to address the need of non-English speaking patients throughout the province of British Columbia. Translation of drug handouts for chemotherapy agents is the focus of the pilot project. According to the 2006 Census, 12.4% of the BC population reported Chinese (8.5%) or Punjabi (3.9%) as their native language; approximately one in five of these individuals have no working knowledge of English.

BENEFIT DRUG LIST

The following program has been added on the benefit list effective 01 September 2011:

- **Pazopanib** (case-by-case) as palliative therapy for renal cell carcinoma (UGUPAZO)

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
UGUPAZO	☑	☑	☑	Palliative Therapy for Renal Cell Carcinoma Using Pazopanib

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJACTT	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Adjuvant Therapy for Breast Cancer using DOXOrubicin and Cyclophosphamide followed by PACLitaxel and Trastuzumab
BRAJACTTG	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: DOXOrubicin and Cyclophosphamide followed by PAClitaxel and Trastuzumab
UBRAJDCT	☐	☑	☐	*Revised timing of MUGA scan or echocardiogram; deleted bili, AST, ALT prior to 1st cycle of DOCEtaxel due to redundancy with baseline lab work; Treatment section revised to include space for dosing weight for trastuzumab; reformatted for TALLman lettering*	Adjuvant Therapy for Breast Cancer Using DOCEtaxel, Carboplatin and Trastuzumab
BRAJDTFEC	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab; reformatted for TALLman lettering*	Adjuvant Therapy for Breast Cancer Using DOCEtaxel and Trastuzumab, and Fluorouracil, Epirubicin and Cyclophosphamide
UBRAJFECDT	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab; reformatted for TALLman lettering*	Adjuvant Therapy for Breast Cancer using Fluorouracil, Epirubicin and Cyclophosphamide followed by DOCEtaxel and Trastuzumab
BRAJTR	☑	☑	☐	*Minor typo in Eligibility corrected in Protocol, Treatment section revised to include space for dosing weight for trastuzumab*	Adjuvant Therapy for Breast Cancer Using Trastuzumab (HERCEPTIN®) Following the Completion of Chemotherapy (Sequential)

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
UBRAVTCAP	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab and Capecitabine
BRAVTPC	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab, PAClitaxel and CARBOplatin as First-Line Treatment for Advanced Breast Cancer
BRAVTR	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab
BRAVTRAD	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab and DOCEtaxel as First-Line Treatment for Advanced Breast Cancer
BRAVTRAP	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Therapy for Metastatic Breast Cancer Using Trastuzumab and PAClitaxel as First-Line Treatment for Advanced Breast Cancer
BRAVTRNAV	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Therapy for Metastatic Breast Cancer Using Trastuzumab and Vinorelbine
BRLAACDT	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Treatment of Locally Advanced Breast Cancer using DOXOrubicin and Cyclophosphamide followed by DOCEtaxel (TAXOTERE®) and Trastuzumab
UGIGAVCCT	☐	☑	☐	*Treatment section revised to include space for dosing weight for trastuzumab*	Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma using CISplatin, Capecitabine and Trastuzumab
UGIAVCETIR	☑	☐	☐	*Typo fixed under Treatment section*	Third Line Treatment of Metastatic Colorectal Cancer Using Cetuximab in combination with Irinotecan
UGIGAVCFT	☐	☑	☐	*Treatment section revised to include space for dosing weight*	Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma using CISplatin, Infusional Fluorouracil and Trastuzumab
GIGAVTR	☐	☑	☐	*Treatment section revised to include space for dosing weight*	Continuation of Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma using Trastuzumab

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
UGIPNSUNI	☑	☐	☐	*Added information on management of SUNItinib-related hypothyroidism*	Palliative Treatment of Advanced Pancreatic Neuroendocrine Tumours using SUNItinib (SUTENT®)
GIRCRT	☑	☑	☑	*Revised treatment schedule of capecitabine*	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Capecitabine and Radiation Therapy
GOOVCADR	☑	☐	☐	*Eligibility clarified*	Second Line Treatment Using DOCEtaxel and CARBOplatin for Epithelial Ovarian Cancer Relapsing after Primary Treatment
GOOVPLDC	☑	☐	☐	*Eligibility clarified*	Second Line Treatment Using Pegylated Liposomal DOXOrubicin (PLD) and CARBOplatin for Epithelial Ovarian Cancer Relapsing after Primary Treatment
UGUSUNI	☑	☐	☐	*Added information on management of SUNItinib-related hypothyroidism*	Palliative Therapy for Renal Cell Carcinoma Using SUNItinib
LUAVDOC	☐	☑	☐	*Liver function tests clarified*	Second-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with DOCEtaxel
ULYALEM	☑	☐	☐	*Revised minor typo in Tests section*	Treatment of Fludarabine-Refractory B-Chronic Lymphocytic Leukemia (B-CLL) and T-Prolymphocytic Leukemia (T-PLL) with Alemtuzumab
SAAVGEMD	☑	☐	☐	*Updated References*	Second or Third Line Therapy for Soft Tissue Sarcomas using Gemcitabine and DOCEtaxel

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

Contact Information	Phone	Fax	Email
Systemic Therapy Update Editor	604.877.6277		mdelemos@bccancer.bc.ca
Provincial Systemic Therapy Program	604.877.707.5973		ldasilva2@bccancer.bc.ca
Communities Oncology Network (CON)	250.519.5501		jdenduyf@bccancer.bc.ca
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		
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