

Systemic Therapy Update



BC Cancer Agency

CARE + RESEARCH

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EDITOR'S CHOICE

2011-2012 NEW DRUG PROGRAM

Gastrointestinal:

The **Provincial Systemic Therapy Program** has approved **capecitabine** and **oxaliplatin** as combination therapy for the adjuvant treatment of resected stage III (node positive) rectal cancer (**UGIRAJCOX**). UGIRAJCOX is an alternative treatment option to FOLFOX (UGIRAJFFOX). This is extrapolated from data for capecitabine and oxaliplatin in high-risk, stage III colon cancer patients. In this patient population, 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;29:1465)

Genitourinary:

The **Provincial Systemic Therapy Program** has approved **abiraterone**, in combination with prednisone (**UGUPABI**), for the treatment of metastatic, castration-resistant prostate cancer (mCRPC) after failure of DOCEtaxel therapy. In a phase III trial, 1196 men whose disease progressed

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with DOCeTaxel were randomized to prednisone alone or the combination of abiraterone and prednisone. The trial was terminated early as abiraterone significantly increased overall survival (OS) (14.8 mo vs. 10.9 mo, HR 0.65, 95% CI 0.54-0.77) at a median follow-up of 13 months, at the time of the interim analysis. (*de Bono et al. NEJM 2011;264:1995-2005*)

Application to and approval by the BCCA Compassionate Access Program (CAP) is required for all *NEW* patients effective 01 November 2011. Patients who had previously received abiraterone through ZAP, the manufacturer's (Janssen Canada) drug access program, prior to 01 November 2011 will continue to access the drug through ZAP. In addition, patients who had previously accessed the drug through the Health Canada Special Access Programme (SAP) may be enrolled into Janssen's ZAP program until 30 November 2011. *Prescribing physicians must enrol these patients prior to the 30 November 2011 deadline.* For information on the drug properties of abiraterone, please refer to the [Cancer Drug Manual](#) section of the current issue of the Systemic Therapy Update.

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

Breast:

The **Breast Systemic Tumour Group** is replacing the **BRAVTRNAV** protocol with **BRAVTRVIN** for the use of trastuzumab and vinorelbine in the palliative treatment of metastatic breast cancer. Compared to the weekly administration schedule of BRAVTRNAV, BRAVTRVIN is associated with a more convenient administration schedule of every 21 days. According to a recent phase III study (HERNATA study) of patients with locally advanced or metastatic HER2-positive breast cancer, the combination of vinorelbine (on days 1 and 8) and trastuzumab (on day 1) every 3 weeks was associated with a median time to progression (TTP) of 15.3 months, a median overall survival of 38.8 months, and a 1-year survival rate of 88% (*Andersson et al. JCO 2011;29:264-71*). Although the two treatment schedules have not been directly compared, the weekly dosing schedule of BRAVTRNAV was associated with a median TTP of 8.5 mo in the TRAVIOTA study. (*Burstein et al. Cancer 2007;110:965-972*)

Patients currently on the BRAVTRNAV protocol may continue this treatment schedule if this is preferred by the patient and/or their oncologist. All new patients for whom vinorelbine and trastuzumab is indicated should be started on the new BRAVTRVIN protocol.

Gastrointestinal:

The **Gastrointestinal Tumour Group** has revised the eligibility criteria for the use of **long-acting octreotide (SANDOSTATIN LAR[®])** in the symptomatic management of neuroendocrine tumours (NETs) of the gastrointestinal tract (**UGIOCTLAR**). Until now, only monthly doses higher than 30 mg required approval via the BCCA Compassionate Access Program (CAP). Effective 01 November 2011, CAP approval is required for all *NEW* prescriptions of long-acting octreotide regardless of dose (not required for refill prescriptions). Annual re-approval for all patients is also required to ensure that individuals who were previously started on long-acting octreotide while asymptomatic do not continue treatment beyond tumour progression. Prescribing physicians are responsible for the annual CAP re-submission based on the approval end-date indicated on the previous CAP request. For patients who are being treated outside a BCCA centre and whose progress notes are not available in CAIS (Cancer Agency Information System), CAP requests should be accompanied with notes documenting the patient's NET-related symptoms.

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The new requirement for CAP approval is due to a 226% increase in utilization of long-acting octreotide in British Columbia over the past 5 years despite the incidence of NETs remaining relatively stable. A recent drug use evaluation conducted by BCCA Pharmacy showed that 26% of new patients starting long-acting octreotide did not display disease-related symptoms at the time of treatment initiation. Although recent data suggest that long-acting octreotide may also delay disease progression in patients with asymptomatic NETs, this indication is not currently funded by the BCCA and is under review by the Gastrointestinal Tumour Group. (Rinke *et al. J Clin Oncol* 2009;27:4656-4663)

EDUCATION CORNER

FAQ: USE OF PROBIOTICS DURING CHEMOTHERAPY TREATMENT

Are Probiotic Supplements Effective For Preventing Chemotherapy-Induced Diarrhea (CID)?

There is insufficient evidence to support the use of probiotics for CID. Probiotics have shown promise in the prophylaxis of CID in case reports, animal studies and one recent human study by Osterlund *et al.*² The study compared *Lactobacillus rhamnosus* to fibre for the prevention of diarrhea in patients receiving fluorouracil.² The Lactobacillus arm showed significantly fewer grades three and four diarrhea (22% versus 37%), and fewer hospitalizations and dose reductions due to bowel toxicity. Further human studies are needed to establish the efficacy of probiotics in CID prevention.

Are Probiotic Supplements Effective For Preventing Chemotherapy-Induced Infections?

There has been recent interest in the medical community in the use of probiotics for the prophylaxis of infections. The putative mechanism is to prevent the translocation of pathogenic bacteria across the gut mucosa.³⁻⁵ However, to date, clinical trials in cancer patients have not demonstrated efficacy in preventing infections.

Is It Safe To Take Probiotic Supplements While Receiving Chemotherapy?

Although probiotics are safe to use in healthy individuals, they can potentially become pathogenic and cause infections in immunocompromised patients. Many patients receiving chemotherapy drugs have weakened immune systems because of chemotherapy-induced leukopenias. A 2006 review conducted by Boyle *et al.* cited 12 cases of bacterial sepsis and 24 cases of fungal sepsis that were likely related to probiotics.⁶ All of the cases occurred in patients with pre-existing morbidities. Patients receiving chemotherapy should *NOT* take probiotic supplements unless they have consulted their oncologist to discuss the risks and benefits.

Is It Safe To Consume Yogurt While Receiving Chemotherapy?

Eating regular yogurt during chemotherapy is generally safe. Yogurts with a probiotic claim often contain higher amounts of live bacterial culture than regular yogurt. It may be prudent to avoid these products until further research is conducted.

Further information on probiotics can be found in the following Health Canada websites:

- [Probiotic Claims in Food](#)
- [Questions and Answers on Probiotics](#)
- [Health Canada Probiotics Monograph](#)
- [About Natural Health Products](#)

EDUCATION CORNER

▪ [Licensed Natural Health Products Database](#)

References:

1. Miller AC, Elamin EM. Use of probiotics for treatment of chemotherapy-induced diarrhea: is it a myth? JPEN J.Parenter.Enteral Nutr. 2009 Sep-Oct;33:573-574.
2. Osterlund P, Ruotsalainen T, Korpela R, Saxelin M, et al. Lactobacillus supplementation for diarrhoea related to chemotherapy of colorectal cancer: a randomised study. Br.J.Cancer 2007 Oct 22;97:1028-1034.
3. Mego M, Ebringer L, Drgona L, Mardiak J, et al. Prevention of febrile neutropenia in cancer patients by probiotic strain Enterococcus faecium M-74. Pilot study phase I. Neoplasma 2005;52:159-164.
4. Mego M, Koncekova R, Mikuskova E, Drgona L, et al. Prevention of febrile neutropenia in cancer patients by probiotic strain Enterococcus faecium M-74. Phase II study. Support.Care Cancer 2006 Mar;14:285-290.
5. Mego M, Majek J, Koncekova R, Ebringer L, et al. Intramucosal bacteria in colon cancer and their elimination by probiotic strain Enterococcus faecium M-74 with organic selenium. Folia Microbiol.(Praha) 2005;50(5):443-447.
6. Boyle RJ, Robins-Browne RM, Tang ML. Probiotic use in clinical practice: what are the risks? Am.J.Clin.Nutr. 2006 Jun;83:1256-64.
7. Health Canada. Drugs and Health Products. Available at: <http://www.hc-sc.gc.ca/dhp-mps/prodnatur/about-appropos/cons-eng.php>. Accessed Jul 28, 2011.

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MEDICATION SAFETY UPDATE

TALLMAN LETTERING IN BCCA PHARMACY LABELS

Pharmacy has adopted **TALLman lettering for all prescription labels at the BC Cancer Agency** effective 28 October 2011. This initiative is part of a BCCA risk reduction strategy to minimize the unintended interchange of Look-Alike/Sound-Alike drugs (as outlined in the BCCA Provincial Pharmacy Directive – *Use of TALLman Lettering for Medication Nomenclature*). Information on this medication safety initiative was previously described in the March 2011 edition of the Systemic Therapy Update (<http://www.bccancer.bc.ca/HPI/stupdate.htm>).

Healthcare professionals and patients at the BC Cancer Agency can expect to see TALLman lettering on labels of parenteral and oral drugs to help distinguish the following drug names:

vinBLAS ^t ine and vinCRIS ^t ine	DOXORub ⁱ c ⁱ n and IDARub ⁱ c ⁱ n
CARBOplatin and CISplatin	inFLIXimab and riTUXimab
DOCEtaxel and PACLitaxel	mitoXANTRONE*
SORAFenib and SUNItinib	cycloSERINE and cycloSPORINE
DAUNORub ⁱ c ⁱ n and DOXORub ⁱ c ⁱ n	dimenhydrINATE and diphenhydrAMINE

**To distinguish from mitomycin and mitotane*

This list is derived from recommendations for TALLman lettering in Oncology drugs by the Institute for Safe Medication Practices (ISMP) Canada. Please visit the following website for the associated ISMP Canada Safety Bulletin: <http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2010-08-TALLmanforOncology.pdf>.

CANCER DRUG MANUAL

NEW MONOGRAPH

Abiraterone Monograph and Patient Handout have been completed. Expert review was provided by Dr. Kim Chi (GU Tumour Group Chair) and Victoria Kletas (GU Tumour Group Pharmacist). Abiraterone is indicated for metastatic castration-resistant prostate cancer after DOCETaxel failure, at the recommended dose of 1 g orally once daily.

Abiraterone is a novel CYP 17 enzyme inhibitor that reduces androgen production in the testes, adrenals and prostate tumour. When used in addition to androgen deprivation therapies (luteinizing hormone releasing hormone [LHRH] agonists or orchiectomy), abiraterone further decreases androgen production to below castrate levels.

The main side effects involve mineralocorticoid effects due to the compensatory increase in cortisol levels through the adrenocorticotrophic hormone (ACTH) feedback on the pituitary gland. Patients with pre-existing cardiovascular disease are at risk of worsening hypertension, hypokalemia and fluid retention. Caution is advised if patients need to be withdrawn from prednisone, which can also increase ACTH. Spironolactone should not be the diuretic of choice. It is a potassium-sparing diuretic which may stimulate the androgen receptor and cause disease progression.

Elevations in liver function tests (AST or ALT greater than 5 X upper limit of normal [ULN] and bilirubin greater than 1.5 X ULN) may occur in the first three months of treatment. Liver function tests should be closely monitored at this time. These elevations may be reversible by reducing the dose or withholding treatment. Please follow the dosing adjustment guidelines as per the UGUPABI chemotherapy protocol.

REVISED MONOGRAPHS

Trasuzumab Monograph has been revised to update the FDA Pregnancy Category to Category D as cases of oligohydramnios have been reported in pregnant women exposed to trastuzumab. Effective contraception is recommended during and for six months after treatment. Other revisions include:

- Addition of gastric cancer as a Health Canada approved indication in the Uses section
- Revisions of the Side Effects table, Supply and Storage, Solution Preparation and Compatibility, and Dosing sections as per current template standard

BENEFIT DRUG LIST

NEW PROGRAMS

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

- **Abiraterone** (case-by-case) and prednisone for palliative treatment of metastatic, castration-resistant prostate cancer after failure of DOCETaxel therapy (UGUPABI)

BENEFIT DRUG LIST

- **Capecitabine** and **Oxaliplatin** (case-by-case) for adjuvant treatment of stage III rectal carcinoma (UGIRAJCOX)
- **Trastuzumab** and **Vinorelbine** (class II) for palliative treatment of metastatic breast cancer using 3-weekly vinorelbine (BRAVTRVIN)

REVISED PROGRAMS

The following programs have been revised on the benefit list effective 01 November 2011:

- **Octreotide** (case-by-case) for symptomatic management of functional neuroendocrine tumours of the GI Tract (UGIOCTLAR)
- **SUNItinib** (class II) for second line treatment of advanced c-kit positive gastrointestinal stromal cell tumours (GIST's) after imatinib (SAAVGS)
- **Yttrium-90** (case-by-case) for transarterial radioembolisation (UGIYTT)

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
BRAVTRVIN	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Palliative Therapy For Metastatic Breast Cancer Using Trastuzumab and 3-Weekly Vinorelbine
UGIAJCAPOX	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Adjuvant Combination Chemotherapy for Stage III and Stage IIB Colon Cancer Using Oxaliplatin and Capecitabine
UGIRAJCOX	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer Using Oxaliplatin and Capecitabine
UGUPABI	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Palliative Therapy for Metastatic Castration Resistant Prostate Cancer Using Abiraterone and Prednisone After Failure of DOCEtaxel Therapy

REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED):					
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVNAV	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Hepatic dose modifications revised</i>	Palliative Therapy for Metastatic Breast Cancer using Vinorelbine
UCNBEV	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Reformatted to standardized template</i>	Palliative Therapy for Recurrent Malignant Gliomas Using Bevacizumab
UGIOCTLAR	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Eligibility revised to require CAP approval and reformatted to standardized template</i>	Symptomatic Management of Functional Carcinoid and Neuroendocrine Tumors of the GI Tract Using Octreotide
GICART	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Minor typos corrected in Treatment and Precautions sections</i>	Combined Modality Therapy for Carcinoma of the Anal Canal using Mitomycin, Capecitabine and Radiation Therapy
UGIYTT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Added requirement for CAP approval to Eligibility section; updated Exclusions section</i>	Yttrium-90 for Transarterial Radioembolisation (TARE)
SAAJGI	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Replaced SGOT by AST in Tests section and reformatted according to standardized template</i>	Adjuvant Treatment of C-Kit Positive High Risk Gastrointestinal Stromal Cell Tumours Using Imatinib
SAAVGI	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Replaced SGOT by AST in Tests section and reformatted according to standardized template</i>	Treatment of Advanced c-Kit Positive and C-Kit Negative Gastrointestinal Stromal Cell Tumors (GIST's) Using Imatinib
SAAVGIDD	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Replaced SGOT by AST in Tests section and reformatted according to standardized template</i>	Treatment of Advanced C-Kit Positive Gastrointestinal Stromal Cell Tumors (GIST's) Using 800mg Dosing of Imatinib
SAAVGS	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Revised Eligibility Section and reformatted to standardized template</i>	Second Line Treatment of Advanced C-kit Positive Gastrointestinal Stromal Cell Tumours (GIST's) After Imatinib Using SUNlitinib (SUTENT®)
SMPTD	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Added information on the need to fill order at BCCA Vancouver Centre and reformatted to standardized template</i>	Topical Therapy for Skin Cancer with PDT (Photodynamic Therapy)

DELETED Protocols, PPPOs and Patient Handouts (AFFECTED DOCUMENTS ARE CHECKED):				
CODE	Protocol	PPPO	Patient Handout	Protocol Title
BRAVTRNAV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Palliative Therapy For Metastatic Breast Cancer Using Trastuzumab And Vinorelbine

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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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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