Editor's Choice: New Treatment Protocols for Lung Cancer

Cancer Drug Manual – New and Revised Monographs: Bleomycin, Gefitinib


Focus on – Aprepitant

Nursing Update: Continuing Competency in Chemotherapy, Article of the Month

Provincial Systemic Therapy Policies – Use of Dimethylsulfoxide (DMSO) in Extravasation Policy

List of New and Revised Protocols

List of New and Revised Pre-Printed Orders

Website Resources: Reimbursement and Forms; Cancer Management Guidelines; Unconventional Cancer Therapies Manual

Editor’s Choice

New Treatment Protocols

The Lung Tumour Group has introduced five new regimens this month. The first three are platinum-based combination chemotherapy for first-line treatment of advanced non-small cell lung cancer using:

- Cisplatin or carboplatin in combination with gemcitabine (LUAVPG).
- Carboplatin in combination with paclitaxel (LUAVCAT).
- Cisplatin in combination with docetaxel (LUCISDOC).

These doublets (two-drug combinations) have similar efficacy based on prospective, randomized peer reviewed data. The existing BCCA protocol of cisplatin and vinorelbine (LUNAVP) differs from these new doublets by dividing the cisplatin dose to reduce toxicity. Based on BCCA data from a phase II trial, the LUNAVP regimen survival data appears similar to the other doublets. The increased number of chemotherapy regimes provides flexibility to clinicians and patients. Treatment can be tailored to individuals to provide convenience and minimize toxicity. Some notable differences between these doublets include:

- LUAVPG causes more anemia and thrombocytopenia.
- LUAVCAT
  - causes more neuropathy
  - administered once every three weeks compared to day 1 and 8 for LUNAVP and LUAVPG. Once every three week chemotherapy delivery is more convenient for patients commuting from a distance.
  - all taxane containing regimens cause more alopecia.
- LUCISDOC
  - may cause more febrile neutropenia and is restricted to ECOG performance status of 0 and 1 only
  - administered once every three weeks compared to day 1 and 8 for LUNAVP and LUAVPG. Once every three week chemotherapy delivery is more convenient for patients commuting from a distance.
  - all taxane containing regimens cause more alopecia.
- The existing LUNAVP
  - least expensive
  - may be associated with more constipation
None of these doublet regimens is suitable for administration with concurrent radiotherapy. LUPE (cisplatin/etoposide) is the only regimen suitable for concurrent chemoradiation in selected stage III NSCLC.

ASCO 2003 guidelines state “Selection of the regimen of choice should be made on the basis of experience, convenience, toxicity and cost.”

The fourth protocol introduced this month is single agent topotecan (LUAVTOP) as second-line treatment in patients with recurrent small cell lung cancer after progression from first-line chemotherapy. Single-agent oral etoposide (LUPOE) is a less toxic alternative to topotecan.

Finally, the cisplatin/gemcitabine protocol for malignant mesothelioma has been implemented (LUMMPG). In October 2004, the cisplatin/pemetrexed (LUCISPEM) protocol was also introduced and made available as a Class II indication for patients with malignant mesothelioma. The LUMMPG and the LUAVPG protocols (see above) have now replaced the previous LUPG protocol which was used for both the mesothelioma and NSCLC populations.

**CANCER DRUG MANUAL**

**New Gefitinib (Iressa®) Monograph** This is now available in conjunction with the existing patient information handout.

**Completely Revised Bleomycin Monograph and Patient Handout** These have been extensively updated to reflect the current usage of this agent.

**Limited Revision of Aromatase Inhibitors’ Patient Handouts** The patient information handouts for the three aromatase inhibitors – anastrozole, exemestane, letrozole – have been revised to include information referring the patient to consult the guidelines for the prevention of osteoporosis developed by the Breast Tumour Group. For more details on the guidelines, see Systemic Therapy Update November 2004.

**PATIENT EDUCATION**

**New and Revised Patient Handouts on Cancer Drugs** The patient information handouts for anastrozole, bleomycin, exemestane, gefitinib and letrozole have been revised. See under Cancer Drug Manual for more details.

**New Patient Handout on Breast Cancer Treatment** A new patient information handout has been developed for the combination adjuvant chemotherapy BRCAFPO protocol for advanced or inflammatory breast cancer. This regimen involves the use of oral cyclophosphamide, doxorubicin and fluorouracil.

**Patient information handouts for cancer drugs** are available on the BC Cancer Agency website (www.bccancer.bc.ca/DrugDatabasePt/) under Health Professionals Info, Cancer Drug Manual, Drug Information for the Patient. For treatment protocol specific information, go to the BC Cancer Agency website (www.bccancer.bc.ca) under Health Professionals Info, Chemotherapy Protocols, Information for the Patient.

**FOCUS ON APREPITANT**

The prospect of nausea and vomiting occurring during and after chemotherapy treatment is always a concern for patients. Currently, there are many anti-emetic agents available, including: ondansetron, metoclopramide, prochlorperazine and dexamethasone. The BC Cancer Agency Protocol Summary for Antiemetic Guidelines...
recommend the standard therapy of using a 5HT-3 antagonist (eg, ondansetron) along with dexamethasone for high-moderate emetogenic chemotherapy regimens.(1)

**Aprepitant** is a new anti-emetic agent, belonging to a class called substance P/neurokinin (NK1) receptor antagonists. NK1 is a specific receptor in the brain stem involved only in nausea and vomiting. Aprepitant is a selective antagonist at the NK1 receptor and has no affinity for serotonin, dopamine or corticosteroid receptors.(2) In two multi-centred, randomised double-blind studies, aprepitant has shown to enhance the combined antiemetic activity of ondansetron and dexamethasone in acute and delayed phases of cisplatin-induced emesis.(3,4)

The oral bioavailability of aprepitant ranges from 60-65% and peak plasma concentration is reached in approximately 4 hours. Elimination of the drug is mainly by metabolism. No dose adjustments are required for patients with renal or hepatic insufficiencies. Chronic continuous use has not been studied and is not currently recommended. In clinical trials, aprepitant has been generally well tolerated. Side effects reported during clinical trials (used in conjunction with ondansetron and dexamethasone) have included: asthenia/fatigue, constipation, diarrhoea, hiccups, nausea (after 5 days post-chemo), anorexia and headache.(2)

Aprepitant inhibits the CYP3A4 system. This could result in elevated plasma levels of those drugs metabolized primarily through the CYP3A4 system. Therefore, aprepitant should be used with caution in patients receiving concomitant medications which are metabolized through CYP3A4. Commonly used chemotherapy agents which are metabolized by this route include docetaxel, paclitaxel and etoposide. In clinical studies, however, aprepitant was usually administered with etoposide, vinorelbine or paclitaxel without any dose adjustments.(2, 5)

In Canada, aprepitant is currently available only through the Health Canada Special Access Programme. The commercial release of aprepitant in Canada is tentatively planned for early 2005. Once it is in place, aprepitant can be dispensed from a community pharmacy. Patients will be responsible for the cost of the aprepitant at that time.

Aprepitant is approved by the Health Canada Special Access Programme for use in combination with other antiemetic drugs for the prevention of acute and delayed nausea and vomiting associated with cisplatin-based chemotherapy. Patients must have high dose cisplatin-related nausea and vomiting uncontrolled by other antiemetic regimens before the aprepitant route can be pursued. Currently, the drug is supplied for free by the manufacturer.(6)

The recommended dosage is a three day regimen together with ondansetron and dexamethasone:

<table>
<thead>
<tr>
<th>Day</th>
<th>Aprepitant</th>
<th>Ondansetron</th>
<th>Dexamethasone</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>125 mg PO 60 min pre-chemo</td>
<td>32 mg IV 30 min pre-chemo</td>
<td>12 mg PO 30 min pre-chemo</td>
</tr>
<tr>
<td>2</td>
<td>80 mg PO in the morning</td>
<td>--------</td>
<td>8 mg PO in the morning</td>
</tr>
<tr>
<td>3</td>
<td>80 mg PO in the morning</td>
<td>--------</td>
<td>8 mg PO in the morning</td>
</tr>
</tbody>
</table>

Aprepitant is available as 125 mg or 80 mg capsules. It can be taken with or without food.

The procedure for obtaining aprepitant is as follows:
1. Patient must be on a cisplatin-based protocol and have nausea and vomiting uncontrolled by other antiemetic regimens.
2. The physician must complete a Health Canada Special Access Request form and fax to the number listed on the form. The physician must specify the hospital pharmacy that the drug is to be delivered to. A copy of the request form is located on the Health Canada website: [www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_sap_drugs_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_sap_drugs_e.html) as well as on the BCCA website: [http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/default.htm](http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/default.htm). Undesignated approval is not required from the BCCA Systemic Therapy Program.
3. Health Canada will review the request. If approval is granted, information will be forwarded to Merck-Frosst Canada. If approval is not granted, the physician will be notified.
4. Merck-Frosst Canada will review the request. If approval is granted, the drug will be shipped to the designated hospital pharmacy. Only one course is dispensed at a time. If approval is not granted, the physician will be notified.
5. The physician must write a prescription for aprepitant, as well as one for ondansetron and dexamethasone. Once supplies have been received, the aprepitant prescription can be filled at the hospital pharmacy at no charge to the patient. The ondansetron and dexamethasone prescriptions are to be filled at the patient’s local community pharmacy. The patient is responsible for the cost of the ondansetron and dexamethasone.
6. The physician must reapply for subsequent cycles.

References:
5. Ginette Sainte-Marie, Personal Communication; Manager, Professional Information; Medical Services; Merck Frosst Canada Inc. Kirkland, Canada. June 2004.

Submitted by
Dawn Annable, BSc(Pharm)
Pharmacy CON Educator
Fraser Valley Centre – BC Cancer Agency

BENEFIT DRUG LIST
The following new programs have been funded by the Provincial Systemic Therapy Program effective 1 December 2004:
- **Carboplatin** (class I) and **paclitaxel** (class II) as first line treatment of advanced non-small cell lung cancer (LUAVCAT)
- **Cisplatin** (class I) and **docetaxel** (class II) as first line treatment of advanced non-small lung cancer (LUCISDOC)
- **Cisplatin** (class I) or **carboplatin** (class I) and **gemcitabine** (class II) as treatment of advanced non-small cell lung cancer (LUAVPG)
- **Topotecan** (class II) as second line treatment of recurrent small cell lung cancer (LUAVTOP)

Where appropriate, a Class II form must be completed and submitted to the Provincial Systemic Therapy Program before the drug will be dispensed at a regional cancer centre or reimbursed to a community hospital.

Ken Swenerton, MD, FRCPC
**ACTING PROVINCIAL SYSTEMIC THERAPY PROGRAM LEADER, BC CANCER AGENCY**

NURSING UPDATE
The end of the year is approaching and some of you are asking questions about meeting the annual requirements for Continuing Competency in Chemotherapy. For those of you who were initially certified before February 2004, you will need to be prepared to show evidence of having met the requirements by February 2005 at the latest. For the rest who were certified after Feb 2004, the date for completing requirements will be one year from the date of initial certification.

We refer you to the following sections of the website for more information about this process.

http://www.bccancer.bc.ca/HPI/Nursing/Education/ChemoEd/ContComp/default.htm

Please call the Nursing Education line at 604-8776098, L. 2638 or toll free 1-800-6633333 L. 2638 if you have questions about this process.
Articles of the month:


*Electronic versions of these articles are accessible within the BC Cancer Agency Regional Center Centers through file: H:EVERYONE\Library\ejournal_intro.htm

Continuing Education Features Available On line:
www: http://www.oesweb.com/
Follow this link to a wealth of print-based continuing oncology nursing offerings including:
• Expanded Applications of Colony Stimulating Factors.
• Molecular Targeted Therapies.
• Cancer Treatment Induced Diarrhea.
• Chemotherapy Induced Nausea and Vomiting.
• Dendritic Cells: Sentry cells of the Immune System.

PROVINCIAL SYSTEMIC THERAPY PROGRAM POLICIES

Policy on Extravasation of Chemotherapy The BC Cancer Agency Systemic Therapy Policy on the Prevention and Management of Extravasation of Chemotherapy (Policy III-20) has been revised in two areas. The first is the addition of intravenous busulfan to the list of vesicants. This agent is mainly used for the conditioning regimen prior to bone marrow transplantation.

The second revision relates to the details on the dose of topical dimethylsulfoxide (DMSO) as an antidote for anthracyclines extravasation. Previously, only the frequency of the application was specified. The revised policy now includes the amount to be applied per surface area to avoid excessive skin reaction. Topical DMSO is commonly suggested as an antidote in extravasation of anthracyclines, although there are inconsistent and sometimes conflicting animal data on its efficacy and safety. A recent review of the published literature found that ulceration was uncommon after anthracycline extravasation when a total of 147 patients were managed with DMSO with or without cooling. When applied appropriately, DMSO seemed well tolerated, with self-limiting local irritation to be the most common adverse effect.

Provincial Systemic Therapy Program Policies are available on the BC Cancer Agency website (www.bccancer.bc.ca) under Health Professionals Info, Chemotherapy Protocols, Policies and Procedures.

LIST OF NEW AND REVISED PROTOCOLS

The INDEX to BC Cancer Agency Protocol Summaries is revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version). Protocol codes for treatments requiring “Undesignated Indication” approval are prefixed with the letter U.

- **LUAVCAT** new: First line treatment of advanced non-small cell lung cancer (NSCLC) with carboplatin and paclitaxel
- **LUAVPG** new (replacing LUPG): Treatment of advanced non-small cell lung cancer (NSCLC) with platinum and gemcitabine
- **LUAOVTOP** new: Second line treatment of recurrent small cell lung cancer (SCLC) with topotecan
- **LUCISDOC** revised (need for undesignated approval changed to class II benefit, eligibility revised): First line treatment of advanced non-small lung cancer (NSCLC) with cisplatin and docetaxel
- **LUMMPG** new (replacing LUPG): Treatment of malignant mesothelioma with cisplatin and gemcitabine
- **LUPG** deleted (replaced by LUAVPG and LUMMPG): Treatment of non-small cell lung cancer and malignant mesothelioma with cisplatin and gemcitabine

**LIST OF NEW AND REVISED PRE-PRINTED ORDERS**

Pre-printed orders should always be checked with the most current BC Cancer Agency protocol summaries. The BC Cancer Agency Vancouver Centre has prepared chemotherapy pre-printed orders, which can be used as a guide for reference. An index to the orders can be obtained by Fax-back.

- **BRAJCEF** revised (revised for clarity): Adjuvant therapy for breast cancer using cyclophosphamide, epirubicin and fluorouracil
- **BRINFCEF** revised (revised for clarity): Therapy for inflammatory breast cancer using cyclophosphamide, epirubicin and fluorouracil
- **BRLACEF** revised (revised for clarity): Therapy for locally advanced breast cancer using cyclophosphamide, epirubicin and fluorouracil
- **GOCXCAD** revised (maximum number of cycles clarified): Treatment of advanced/recurrent non-small cell cancer of the cervix with carboplatin and docetaxel in ambulatory care settings
- **GOENDCAD** revised (maximum number of cycles clarified): Treatment of primarily advanced or recurrent endometrial cancer using carboplatin and Docetaxel
- **GOOVCADR** revised (maximum number of cycles clarified): Second line treatment using docetaxel and carboplatin for epithelial ovarian cancer relapsing after primary treatment
- **GOOVCADX** revised (maximum number of cycles clarified): Primary treatment of visible residual (extreme risk) invasive epithelial ovarian cancer
- **LYCVPR** revised (appointments section for Cycle #1): Treatment of Lymphoma with Doxorubicin, Cyclophosphamide, Vincristine, Prednisone and Rituximab (CHOPR)

**WEBSITE RESOURCES**

Reimbursement and Forms: The current Benefit Drug List, Class II forms and Undesignated Indication Application forms are available on the BC Cancer Agency website under Health Professionals Info, Chemo-therapy Protocols, Frequently Used Forms (http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms.htm).


The Cancer Chemotherapy Protocols are available on the BC Cancer Agency website (www.bccancer.bc.ca/ChemoProtocols) under Health Professionals Info, Chemotherapy Protocols.

The **Unconventional Cancer Therapies Manual** is available on the BC Cancer Agency website www.bccancer.bc.ca under Patient/Public Info, Unconventional Therapies.

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 UPDATES  Please ☑ Fax-Back information below:

***Most items have been hyperlinked for easy access***

| ☐ All items for December 2004 (Vol 7 № 12) |
| Cancer Drug Manual Monographs: (also available on our website www.bccancer.bc.ca) |
| ☐ bleomycin  ☐ gefitinib |
| Patient Education Handout: (also available on our website www.bccancer.bc.ca) |
| ☐ anastrozole  ☐ bleomycin  ☐ exemestane  ☐ gefitinib  ☐ letrozole |
| Pre-Printed Orders: |
| ☐ BRAJCEF  ☐ BRINFCEF  ☐ BRLACEF  ☐ GOOVCADR  ☐ GOOVCADX  ☐ GOCXCAD  ☐ GOENDCAD  ☐ LYCVPR |
| Protocol Summaries: (also available on our website www.bccancer.bc.ca) Index of Protocol Summaries |
| ☐ LUAVCAT  ☐ LUAVPG  ☐ LUAVTOP  ☐ LUCISDOC  ☐ LUMMPG |
| Provincial Systemic Therapy Program Policies |
| ☐ Prevention and Management of Extravasation of Chemotherapy (Policy III-20) |
| Reimbursement (also available on our website www.bccancer.bc.ca) |
| ☐ Benefit Drug List (01 December 2004)  ☐ Class 2 Form (01 December 2004) |
| Systemic Therapy Update Index (also available on our website www.bccancer.bc.ca) |
| ☐ Jan-Dec 2000  ☐ Jan-Dec 2001  ☐ Jan-Dec 2002  ☐ Jan-Dec 2003 |

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