HOT SPOT

Editor's comments

At the start of this new year it is appropriate that we take a moment to reflect on the past year. For the Rapid Response Radiotherapy Program (RRRP) it has been an exciting and eventful year. We introduced new services, enhanced existing ones, and expanded our program.

Over the past year we increased the number of half-day palliative radiotherapy clinics and now have a clinic every day of the week. In January we started a prospective database, which now contains over 400 patients. We completed two surveys, initiated seven research protocols, and presented six posters at national and international meetings. We have eight abstracts accepted for presentation in the upcoming Palliative Care 10th Annual Conference on March 26-28, 2000 in Toronto. The results of our referring physicians' survey of RRRP has been accepted for publication in **Supportive Care in Cancer**. In response to the survey's result we now fax our interim report on the day of consultation in addition to giving a copy to the patient. The S&WCHSC Palliative Care Initiative (PCI) under the direction of Dr. Librach should help address the problem of poor accessibility to palliative care services in general, which was one of the identified weaknesses in that survey. The survey on patterns of practice for palliation of bone metastases in Canada was presented at national and international meetings. We received five grants (two internal and three external) to fund our research projects. Patients referred to the RRRP are offered the opportunity to participate in collaborative trials (RTOG – bone metastases, or PMH – renal study) or in-house studies (radiotherapy with/without Pamidronate, Fentanyl for control of incident pain, patient's expectation, and CT bone density measurements). The report of a workshop on research methods in palliative radiation oncology organized by us in collaboration with the PMH was published in **Current Oncology**. We participated in the Pain and Symptom Management Conference conducting a palliative radiotherapy workshop in Toronto in November. Our monthly educational rounds are being approved for the Royal College maintenance of certification. We offer a half-day elective for community health care professionals interested in learning about our program. At the university, we offer an elective in palliative radiotherapy for medical students.

With our dedicated orthopedic colleagues (Drs. Axelrod, Finkelstein and Stephen) we started a multidisciplinary bone metastases clinic, the first of its kind in Canada, which is described in Lou Andersson's article in the **Canadian Oncology Nursing Journal**. Our experience with the first 100 patients will be analyzed and presented later this year. We are in the process of implementing percutaneous cementoplasty in the clinic.

We published four issues of **Hot Spot** and added an insert to the last three issues. The inserts were on the management of pain, malignant wounds, and GI toxicities. Our newsletter has improved communication with our referring physicians. We expanded our editorial board and have added regular columns to our newsletter on psychosocial, ethical issues, what's new in metro palliative care and at the PMH palliative radiotherapy program. A new column "Ask the Experts" aims to answer your questions. Please submit your questions to Dr. Cyril Danjoux. Dr. Charles Hayter will provide a historical perspective – a historical vignette.

We welcome the millennium as an opportunity to improve our program, provide better care to our patients and enhance communication with our community colleagues.

Advance care planning for people with cancer

By Scott Berry, MD, FRCPC

Consider this case: A 74-year-old woman with metastatic breast cancer has been admitted to the hospital because of pneumonia and delirium; she has recently failed third-line chemotherapy. She needs antibiotics and may need admission to the intensive care unit if her respiratory condition deteriorates. She is not competent to make any decisions regarding medical treatment at the time of admission. Her husband is there, but when you talk to him, he tells you that he and his wife have never talked about whether she would want to be on a "breathing machine" if she became very ill.

Have you found yourself in a situation like this? It is not uncommon and can be very distressing for everyone involved. It might be possible to avoid situations like this through "advance care planning".

Advance care planning is a "process of communication among patients, health care providers, their families, and important others regarding the kind of care that will be considered appropriate when the patient cannot make decisions".

Advance directives (ADs) are documents that can be an important part of this process. They are helpful because they

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HOT SPOT

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The emotional needs of the person with advanced cancer

By Mary L.S. Vachon, RN, PhD

In a large study of the needs of persons living with cancer in four Canadian provinces, 61-79% of those with terminal illness, compared with 18-34% of the general cancer population, reported significant distress. Of patients who reported distressing to excruciating pain in the past week, 69-100% reported significant distress. The problems associated with high distress are shown in Table One.

Five to 15 per cent of the general cancer population experiences major depression, while 6 to 25% of those with terminal illness experience a clinical depression. The desire for an early death in those with advanced disease was associated with depression, pain and low social support.

Quality of life scores in those with advanced cancer were strongly associated with survival in a number of studies and carried prognostic significance independent of conventional measures. There is evidence that a person's perceived quality of life may influence survival.

One aspect of quality of life is the maintenance of hope. In discussing advanced disease, it is important to always maintain some degree of hope. Ideally such discussions should take place over time and allow for ongoing dialogue between the clinician and the patient. Taking away all hope in the early stages of diagnosis or with the diagnosis of advanced disease is destructive to patients and to their trust in the ability of the health care system to care for them. The destruction of hope by the health care professional not infrequently leads to patients turning to complementary health care, sometimes with positive results.

Over the course of illness, and with the support of a caring health care team, hope may change from hope for a cure, to improved symptom relief, to finding meaning in one's life and in one's illness, to resolving previous conflicts or spiritual and existential distress, to not being abandoned by those who care for us - family, friends and the treatment team, to dying in a way that is congruent with how we lived. The hope to live longer can be exchanged with the hope to live in a meaningful way, finding a purpose in suffering, and peace of mind while dying. Effective team work can facilitate this process for patients and their families.

Table One: Determinants of distress in patients with advanced cancer pain

Impaired role performance

- caring for an elderly relative
- work activities
- relationship with friends
- role as a partner
- inability to engage in usual religious practices
- household activities
- social activities
- relationship with partner
- role as a parent

Illness-related fears

- about dying
- about recurrence of disease

Other symptoms and side effects

- problems with seeing or hearing
- feeling tired
- cognitive impairment
- lack of energy
- loss of interest in food
- gastrointestinal symptoms

Advanced care planning for people with cancer

continued from page 1...

allow a person, while competent, to indicate who they would want to make treatment decisions on their behalf and/or what treatments they would want if they became incompetent. ADs are also known as "living wills" or, in Ontario, "powers of attorney for personal care". Original AD documents, such as "The University of Toronto Centre for Bioethics Living Will", were intended for the general public. The Centre For Bioethics' Living Will is a booklet with chapters on general questions and answers about ADs, the legal status of ADs, information about health care decisions, information about personal care decisions, the AD form itself, and an identification card. The AD chapter includes both a proxy directive (i.e. the portion which indicates who a patient would like to make decisions for them) and an instruction directive (the portion which indicates what treatments the person would want in the future). The instruction directive contains a grid in which a person can indicate which treatments he would or would not want in different health states by indicating yes, no, undecided or treatment trial in each cell of the grid. These "generic" documents contained hypothetical, often irrelevant choices and inadequate prognostic information for people with cancer.

Dr. Peter Singer, director of The University of Toronto Joint Centre for Bioethics, developed the concept of disease-specific ADs. Disease-specific ADs have several advantages over their generic counterparts. First, they present patients with scenarios and treatments that the patient is likely to confront. Second, because the group of patients completing the AD document is more homogenous, more specific prognostic information can be presented. Finally, because the patient already has experience of the illness which may lead to those choices, the choices themselves are less hypothetical.

A cancer-specific advance directive has been developed and evaluated in a study of 90 oncology outpatients by Berry and Singer. The "Cancer Living Will" was adapted from the University of Toronto Centre for Bioethics Living Will. The primary difference between the Centre For Bioethics Living Will and the Cancer Living Will is the chapter containing information about health care decisions which incorporates descriptions of "health states" in which the AD may be needed and treatments that might be required while in those health states. The description of health states and treatments in the Cancer Living Will refers specifically to issues in the care of people with cancer while the Centre For Bioethics Living Will is more general. For instance, in the Cancer Living Will, the description of "Current Health" (which includes the description of acute and potentially reversible illnesses that the person might experience) includes descriptions of hypercalcemia and febrile neutropenia while the Centre For Bioethics Living Will mentions cardiac arrest and pneumonia. The full text of updated versions of both ADs is available at the University of Toronto Joint Centre for Bioethics website (URL: www.utoronto.ca/jcb). Sixty-four per cent of respondents in the study of oncology outpatients preferred the Cancer Living Will to the generic one, generally because of its attention to scenarios and treatments of concern to people with cancer.

Although the Cancer Living Will is an important part of the advance care planning process for people with cancer, some recent empiric research on AD use is informative for clinicians. First, although AD documents might not always be completed, they often stimulate discussion of issues around end-of-life care between patients and their loved ones. Second, physicians are often not part of the discussions around these end-of-life issues because they are thought to be "private". Finally, although preservation of autonomy was an important issue for original developers of ADs, there are other issues of more importance for people taking part in an advance care planning process. In one study, the advance care planning was important to help patients confront death, achieve a sense of control and to relieve burdens on and strengthen relationships with loved ones.

You may be able to help your patients get started on the process of advance care planning by introducing the topic to them. ADs such as the Cancer Living Will could be useful in introducing the topic and serve as a focus for discussion and planning by patients and their loved ones.

Historical Vignette:

The beginnings of palliative radiotherapy in Canada

By Charles Hayter, MA, MD, FRCPC, Radiation Oncologist, T-SRCC

Radiation therapy in Canada has a history that goes back almost 100 years to the discovery of x-rays in 1895 and radium in 1898. Within a few years, both these modalities were found to have biological effects and were being used to treat human disease.

Physicians were particularly interested in the effects of radiation on cancers. It was quickly discovered that radiation could not only cure cancer, but also relieve pain and other symptoms when cure was impossible. The first Canadian physician to report on the use of x-rays to treat cancer, Abraham Groves of Fergus, Ontario *(photo, top right)*, was impressed in 1902 by the good palliation of two patients with advanced uterine cancer. The following year, Toronto x-ray pioneer John McMaster wrote: "opiates may be laid aside very soon after beginning x-ray treatment."

Canada's foremost radiotherapist in the early years of the twentieth century was Dr. William H. B. Aikins (1859-1924), an 1881 graduate of U of T *(photo, lower right)*. After visiting Paris and witnessing the effects of radium on disease, he purchased a supply of radium and opened the Radium Institute of Toronto at 134 Bloor Street W. in 1910. At this location he treated patients from across Canada for a wide variety of benign and malignant conditions. In 1916 he was elected first president of the American Radium Society.

Aikins was particularly interested in palliative radiotherapy. He noted that for many patients "the prolongation of life alone would be a doubtful blessing, owing to the distressing symptoms which render life a burden." He felt the greatest benefit that radium had conferred on humanity was the relief it provided to "countless patients whose case is absolutely hopeless from the point of cure." His case reports contain many examples of the successful use of radiation in treating pain, bleeding, or discharge from advanced cancers.

The experiences of physicians such as Groves, McMaster and Aikins laid the foundation for the use of palliative radiotherapy in Canadian medicine.

When does palliative care begin?

By S. L. Librach, MD, CCFP, FCFP, W. Gifford-Jones Professor of Pain Control and Palliative Care, University of Toronto; Director, Palliative Care Initiative, SWCHSC

There is a misconception concerning when palliative care begins and when should it be integrated into a patient's care. There are a number of issues that need to be discussed.

First, there is no distinct dividing line between active, curative-oriented care and palliative care. No one suddenly becomes "palliative" within a course of a progressive illness such as cancer. The time when so-called "curative" treatment ends is often a point of referral to palliative care programs, but that may be far too late to accomplish the tasks of meeting patient and family needs. Palliative care should not be seen as very end-of-life care only. This issue is reflected very well in the standards document of the Canadian Palliative Care Association and in the documents about end-of-life care in the United States and the United Kingdom.

Second, the things that should govern the involvement of palliative care are patient and family needs and expectations. The needs for physical symptom management may require the expert advice of palliative care providers quite early on in the course of the illness. The complex psychosocial and spiritual needs of patients and families may as well require assistance of experienced palliative care providers. There is not a shred of evidence that involving palliative care early on destroys a patient's hope or destroys their urge to "fight" the cancer. This is a myth heard quite often. Early involvement in home palliative care and volunteer hospice programs will lead to better outcomes in the long run.

Third, patients with advanced cancer, and their families, often want to talk about issues of death and dying and begin some advance care planning for end-of-life care. Discussing these issues does not destroy hope, but may actually strengthen patients and families. Discussing these issues is good preventive care for both patients and families and often makes the course at the end of life much more manageable for everyone.

Palliative care needs to be carefully integrated into the continuum of cancer care in Ontario. It is essential to the provision of care to cancer patients and their families. The barriers to this happening need to be explored and removed.

Palliative radiation oncology program at the Princess Margaret Hospital

By Andrea Bezjak, MDCM, MSc, FRCPC

The benefit of radiation has long been recognized in palliating symptoms of cancer patients. Indeed, a significant portion of patients seen by radiation oncologists require palliative radiotherapy, either at the time of initial diagnosis or at some later time. Research into palliative radiotherapy is not well established, partially due to the challenges of research in patients with advanced cancer and limited life expectancy. It was with the dual goals of delivering prompt and specialized radiotherapy and performing clinical trials in this area, that the Palliative Radiation Oncology Program (PROP) was started at Princess Margaret Hospital (PMH) in July 1997. The program has been supported in part by funds donated by the family of a previous patient, the late Mr. Allan Kerbel, who wished to bring attention to symptom control and quality of life of patients with incurable cancers.

Nearly 50% of all patients seen in a radiation therapy department are referred for palliative treatment. Since it was not practical to manage such a large number of patients through PROP, we decided to target several common problems: bone metastases, brain metastases, and symptoms related to locally advanced lung cancer. There are currently four randomized studies ongoing for patients being considered for palliative radiation: 1) Single 10 Gy vs 20 Gy in five fractions for palliation of symptoms from lung cancer; 2) Single 8 Gy versus 20 Gy in five fractions for painful bone metastases; 3) Zoledronate (a third-generation biphosphonate) vs. placebo for patients with newly diagnosed bone metastases and a reasonable life expectancy; and 4) Radiation +/- a new radiosensitizer (gadolinium texaphyrin) for treatment of brain metastases in patients with good performance status. We also help to accrue patients onto other studies being conducted at PMH, including a phase II study of higher dose RT for bone metastases from renal cell cancer (often considered radioresistant); and a study of behavioural intervention to help relieve stress in caregivers and improve their coping skills. A study of nutritional supplements for cachexia is planned, and PROP patients may also participate in ongoing trials aimed at relieving dyspnea due to muscle weakness, or opioid-induced dry mouth (two NCIC clinical trials group symptom control studies).

Over the last 22 months (January 1998 to October 1999), 586 patients were seen through PROP and started treatment within a few days; 102 patients agreed to enter clinical trials. Collaboration with our colleagues in RRRP at TSRCC has been particularly satisfying, as exemplified by a successful workshop on issues in palliative radiotherapy held in June 1999 in Toronto, frequent meetings, and planned joint protocols. We welcome this opportunity to contribute to the **Hot Spot** newsletter, a great communication tool to increase our knowledge and awareness of various initiatives within palliative radiotherapy, with the goal of improving quality of care and our patients' quality of life.

Ask the experts:

Recently I sent a patient to the Rapid Response Radiotherapy Program for urgent radiation to his lumbar spine. He had prostate cancer with demonstrated metastases in the lumbar vertebrae causing severe incident pain. Two days following his treatment he abruptly lost motor function in both legs. Could the radiation treatment be responsible for this? Is there a chance of recovery, perhaps with treatment with Decadron?

David Ouchterlony, MD
Palliative Care Specialist
Temmy Latner Centre for Palliative Care
Mount Sinai Hospital, Toronto

Reply...

Radiation therapy can cause edema of the irradiated tumour resulting in increased mass effect. This is particularly important when the tumour is within a confined space and/or adjacent to a critical structure. Clinical examples include irradiation of intracerebral tumours, superior vena caval obstruction, airway obstruction and spinal cord compression. This acute edema (within hours to two to three days), may also account for the flare pain when bony metastases are being irradiated.

In this patient, acute soft tissue edema is the most likely cause for his acute neurological decline. The alternative explanation is acute compression fracture of the vertebrae resulting in cord compression.

The above condition is not due to radiation myelopathy, i.e. direct damage of the spinal cord from the radiation. Radiation damage of the spinal cord does not occur until approximately six months after radiotherapy, after doses in excess of spinal cord tolerance.

Severe intractable back pain can be due to bony metastases alone, (demonstrated on plain x-rays or bone scans), but could also represent pending cord compression, with soft tissue disease causing early cord compression which can be diagnosed by an MRI or CT myelogram.

I would recommend the patient be managed as in any other cases of cord compression, i.e. commencement of Decadron, and imaging with MRI or CT myelogram to determine the cause of the decline. The overall long-term prognosis for neurological recovery is the same as in other circumstances of spinal cord compression, i.e. a patient with rapid complete recovery with Decadron (within 12-24 hours) is likely to maintain neurological function, while patients with only marginal recovery would not be expected to recover. It would be appropriate to consider urgent surgical decompression depending on the patient's general condition and extent of disease.

Rebecca Wong, MBChB, FRCPC,
Radiation Oncologist, Rapid Response Radiotherapy Program, Toronto-Sunnybrook Regional Cancer Centre

Research Corner

By Rebecca Wong, MBChB, FRCPC

Unresectable primary rectal cancer and pelvic recurrences from rectal cancer are a significant challenge in terms of palliative management. Despite attempts at preventing local recurrences with the routine use of adjuvant postoperative pelvic irradiation, there remains a population of patients who will recur in the pelvis including patients who, for a variety of reasons (e.g. complications after surgery contraindicating postoperative radiotherapy and or chemotherapy, patient refusal of therapy), did not receive adjuvant radiotherapy. Uncontrolled pelvic disease usually is accompanied by intractable pain, as well as potential risks of fistula formation, bowel and ureteric obstruction.

Palliative radiotherapy has been used extensively for pain relief and symptom control such as bleeding, tenesmus and mucous discharge. Median duration of pain response is in the order of four to six months. Efforts to maximize the effectiveness of radiotherapy include various strategies such as altered fractionation schemes and escalating doses.

Combined modality therapy represents a treatment approach that has been broadly employed in the curative management of many malignancies with proven effectiveness. Combined modality, when used appropriately, can also be efficacious for the management of patients requiring optimal palliation.

Chronotherapy, the delivery of therapy according to the circadian variation of cancer and tumour cells, can reduce the toxicity of therapy and/or allow escalation of therapy to augment its effectiveness.

A phase I study of 5FU leucovorin and pelvic radiotherapy in patients with advanced or recurrent rectal cancer is ongoing at T-SRCC. This study may pave the way for strategies to improve the outcome of patients with unresectable or recurrent rectal cancer. This clinical trial, in collaboration with the University of Florida, employs both combined modality and chronotherapy.

Eligible patients are those with locally advanced or recurrent rectal cancer, (ECOG two, life expectancy greater than eight weeks), who are candidates for pelvic radiotherapy and have not had prior pelvic radiotherapy. The study intervention consists of chronotherapy infusion of 5FU and leucovorin Days One through 25 and concomitant radiotherapy to the pelvis to 4500cGy in 25 fractions (delivered after 12 noon). The primary endpoint is acute toxicity and secondary endpoints include objective response.

It is anticipated that for selected patients, where the natural history of the disease demonstrates that local recurrence is the predominant or sole source of failure, morbidity and mortality, this novel strategy could potentially allow us to provide better, more durable palliation.

For referral of potential candidates for this study, please call new patient bookings at (416) 480-4205. Any queries about this study should be directed to Dr. Rebecca Wong at (416) 480-6165.

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HOT SPOT Prevention and treatment of radiation-induced emesis

Risk Categories	Estimated incidence of emesis	Volume of radiotherapy	Prophylactic treatment	Symptomatic treatments
High	**90%**	**TBI** **Hemibody irradiation**	**$5HT_3$ antagonist**[1]	$5HT_3$ antagonist and steroid or dopamine receptor antagonist
Intermediate	**40-70%**	**Abdomen** **Mantle** **Cranium** **Cranial spinal**	**$5HT_3$ antagonist**[2] **or dopamine receptor antagonist**[3] or steroid[4]	In patients who failed $5HT_3$ prophylaxis: $5HT_3$ antagonist and dopamine receptor antagonist or steroid[5]
Low	**0-30%**	**Breast** **Head and neck** **Extremities** **Pelvis** **Thorax**	**Not usually necessary**	In patients who are symptomatic: dopamine receptor antagonist or phenothiazines or $5HT_3$ antagonist

Notes:

1. $5HT_3$ antagonist (e.g. ondasetron 8mg bid) is very effective for short courses of TBI (total body irradiation) with control rate in the order of 90%. Oral administration is recommended.
2. $5HT_3$ antagonist (e.g. ondasetron 8mg bid) effective in improving emesis rate from 50% to 80% especially for short courses of therapy. The ideal duration of therapy has not been established for prolonged (greater than one week) of radiotherapy.
3. Dopamine receptor antagonist (e.g. domperidone 10 mg tid po, maxeran 10mg tid po)
4. Steroid (e.g. Decadron 2mg tid po) has been shown to be effective when compared with placebo in intermediate risk patients.
5. The combination of Decadron with 5HT3 antagonist is effective in the management of chemotherapy-induced emesis. This strategy has not been proven in randomized controlled trials for radiation-induced emesis, but represents a reasonable option for patients who failed $5HT_3$ antagonist as prophylaxis.

• Bold text represents recommendations in accordance to ASCO 99, MASKCC 98, NCCN 97 antiemetic guidelines.

By Rebecca Wong, MBChB, FRCPC, Radiation Oncologist, Rapid Response Radiotherapy Program, Toronto-Sunnybrook Regional Cancer Centre

Supplement to **Hot Spot**, the newsletter of the **Rapid Response Radiotherapy Program** of Toronto-Sunnybrook Regional Cancer Centre - February 2000
Sponsored by Glaxo-Wellcome

HOT SPOT

Prevention and treatment of chemotherapy-induced nausea and vomiting (N&V)

Level*	Estimated (%) incidence of N&V	Recommended prophylaxis for acute N&V (within day one of chemotherapy) **	Recommended prophylaxis for delayed N&V (after day one)	Comments
Bone marrow transplant	100	$5HT_3$ receptor antagonist given orally - 30 to 60 minutes prior to chemotherapy + Dexamethasone 12mg given orally - 30 to 60 minutes prior to chemotherapy and 12 hours later ± Prochlorperazine 10mg given orally - 30 to 60 minutes prior to chemotherapy	Dexamethasone 4 to 8mg given po bid starting after last chemotherapy	The optimal regimen for prevention of both acute and delayed N&V for transplant patients is not known. Prevention of N&V in this patient group is more difficult than for those receiving highly emetogenic chemotherapy. Further research is ongoing.
5 4 3	90 60 - 90 30-60	$5HT_3$ receptor antagonist given orally - 30 to 60 minutes prior to chemotherapy + Dexamethasone 12mg given orally - 30 to 60 minutes prior to chemotherapy and 12 hours later	Level 5 and 4 Dexamethasone 4 to 8mg po bid for eight doses - starting day after last chemotherapy dose Level 3 Dexamethasone 4 to 8mg given po bid for four doses - starting day after last chemotherapy dose	There is little evidence to support a different approach to the prevention of acute N&V between the top three Hesketh levels. Patients receiving Hesketh Level 3 regimens may be adequately protected with lower doses of a $5HT_3$ receptor antagonist without dexamethasone. Level 3 regimens may not require prophylaxis for delayed N&V in all patients. Further research is needed
2	10 - 30	Prochlorperazine 10mg given orally - 30 to 60 minutes prior to chemotherapy + Dexamethasone 12mg given orally - 30 to 60 minutes prior to chemotherapy	No routine prophylaxis recommended	Patients receiving Hesketh Level 2 regimens who failed non $5HT_3$ receptor antagonist based antiemetic regimens should receive antiemetic Hesketh Level 5 - 3 regimen ± dexamethasone for prevention of delayed symptoms in subsequent chemotherapy cycles
1	< 10	No routine pharmacological prophylaxis recommended	No routine prophylaxis recommended	Patients receiving Hesketh Level 1 regimens who failed conservative measures should receive Hesketh Level 2 antiemetic regimen in subsequent cycles of chemotherapy

* Based on the article by Hesketh PJ. et al. **Journal of Clinical Oncology 1997;15**:103-109

** Prevention of N&V is the goal in all patients receiving cancer chemotherapy. Current pharmacological interventions are more effective at preventing N&V than treating these side effects once they occur.

• For breakthrough N&V Prochlorperazine 10mg given p.o. every four to six hours. If unable to take medication orally, it may be given either rectally or intramuscularly.

Modified Hesketh Level for Chemotherapy Agents

SINGLE AGENTS			COMBINATION		
Drugs	**Dose**	**Level**	**Combination Chemotherapy**	**Emetogenic Level Single Agent**	**Combination**
Cisplatin (P)	≥50 mg/m^2 <50 mg/m^2	5 4	C 600 mg/m^2 M 40 mg/m^2 F 600 mg/m^2	3 1 2	4
Cyclophosphamide (C)	>1500 mg/m^2 >750 mg/m^2 ≤1500 mg/m^2 ≤750 mg/m^2	5 4 3	A 60 mg/m^2 C 600 mg/m^2	3 3	4
Methotrexate (M)	>1000 mg/m^2 250 – 1000 mg/m^2 >50 mg/m^2 < 250 mg/m^2 ≤50 mg/m^2	4 3 2 1	C 750 mg/m^2 H 50 mg/m^2 O 2 mg Prednisone 100 mg	3 3 1 N/A	4
Fluorouracil (F)	<1000 mg/m^2	2	C 1000 mg/m^2 A50 mg/m^2 V 1 mg/m^2	4 3 1	5
Paclitaxel (T)		2	P 75 mg/m^2 T 175 mg/m^2	5 2	5
Doxorubicin (A or H)	20 – 60 mg/m^2	3			
Vinca Alkaloids/Bleomycin		1			

Prepared by Carlo De Angelis, Pharm.D. Department of Pharmacy, Sunnybrook & Women's College Health Science Centre and Toronto-Sunnybrook Regional Cancer Centre

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