

HOT SPOT

The Newsletter of the Rapid Response Radiotherapy Program
of the Odette Cancer Centre



Volume 15, Issue 3, August 2013

Editorial

By Dr. Arjun Sahgal, MD, FRCPC

All hail the new chief of the Department of Radiation Oncology at the Odette Cancer Centre, Dr. Gregory Czarnota. We had tremendous success under Dr. Shun Wong's leadership and look forward to the future of OCC under new leadership and a new vision.

We present to you a special and exciting issue of *Hot Spot*. First, we are proud of Sunnybrook researcher, Dr. Edward Chow, who led a major randomized trial on re-irradiation for painful bone metastases that was presented at ASCO this year. The trial concluded efficacy in re-irradiating patients with painful bone metastases despite failure of a previous first course of radiation. Moreover, this treatment can be given as a one shot treatment that maximizes patient convenience, which is paramount for those at the end stage of their life and suffering from pain. A single fraction was also shown to be better tolerated than multiple fraction

treatments. We congratulate Dr. Chow, the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG), and investigators from nine countries who were able to randomize 850 patients to answer this critical question.

Several controversial issues with respect to end-of-life care and the palliative philosophy are presented in this issue. The work described by Dr. Hyon Kim reflects the continued dedication to excellence in palliative care and education at the Odette Cancer Centre, as she describes an innovative self-care module for palliative care medical learners. Dr. Mary Vachon provides a thoughtful discussion on "Compassion fatigue" which is an interesting area of research, and one we should all be mindful of as caregivers for people facing incurable disease. Dr. Philip Hébert provides an overview of the current status on end-of-life care in Canada and the recent major step

forward the province of Quebec has undertaken to empower patients. From McMaster University, Dr. Marissa Slaven describes their work on hospice stay and patient performance status, which is critical as most patients would rather pass away at home or in a dedicated care facility rather than in a busy hospital. Lastly, Dr. Irene Ying provides an insightful and excellent discussion on "Unrealistic Optimism (UO)", and again an issue we must be mindful of.

The insert has been provided by Dr. Vikas Gupta on myeloproliferative disorders and new therapeutics, and certainly an area in which we will continue to make gains as new therapies emerge, and lastly an overview of the upcoming CME conferences by Dr. Ewa Szumacher.

Welcome the new DRO chief



Hot Spot is delighted to announce that Dr. Gregory Czarnota has been appointed as the new Chief, Department of Radiation Oncology, Sunnybrook Health

Sciences Centre. In addition, Dr. Czarnota will also serve as the Head, Radiation Program at the Odette Cancer Centre. His position was effective July 1, 2013.

Dr. Czarnota is a graduate of the University of Toronto and has been a member of the Sunnybrook team since July 2005 when he was recruited into the Department of Radiation Oncology and as a scientist in

the Sunnybrook Research Institute. Since 2010, he has been the Director, Odette Cancer Research Program, Department of Radiation Oncology and Physical Sciences Research. Since July 2009, he has held the Cancer Care Ontario Research Chair in Imaging and Experimental Therapeutics. Dr. Czarnota is currently an Associate Professor in the Department of Radiation Oncology and in the Department of Medical Biophysics at the University of Toronto.

We would like to thank Dr. Shun Wong who has done an outstanding job of leading the department for 10 years, and welcome Greg, as he assumes this important leadership role!

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Single radiation treatment effective for recurrent pain

Toronto, ON (June 2, 2013) - In the first study of its kind, Sunnybrook researchers report that for patients with bone metastases undergoing a second round of radiation therapy for recurrent pain, single-fraction radiation treatment in one day is as effective, and with less side effects, than multiple-fraction treatment over five days.

Results of this large, randomized study conducted by the NCIC Clinical Trials Group at Queen's University were presented at this year's American Society of Clinical Oncology (ASCO) Annual Meeting. The trial involved 850 patients from nine countries.

"We want to continue to provide efficacious pain management strategies for patients with cancers that have spread to the bone. In tandem with better chemotherapies that are helping patients live longer, for those who still require pain relief after first radiation treatment, we now know that a single-fraction, second treatment is as effective as multiple-fraction second treatment, offering these

patients similar pain control but with less side effects," says Dr. Edward Chow, lead investigator and radiation oncologist, Sunnybrook's Odette Cancer Centre, and professor, Department of Radiation Oncology, University of Toronto, Canada.

The researchers report that benefit from radiation therapy was observed in 45 per cent of evaluable patients who received single-fraction, second radiation treatment (8 Gy in a single day). Benefit from radiation therapy was observed in 51% of evaluable patients who had multiple-fraction second treatment (20 Gy over five days). Based on these data, assessments of how pain interfered with daily activities, and evaluations of quality of life, the investigators concluded that the single treatment was as good as the more complex multiple-day treatment.

While benefit from radiation therapy was similar for both groups and overall survival was the same, the researchers report significantly increased side effects for patients who had multiple-fraction

treatment over five days. Side effects included skin reddening, nausea, lack of appetite, vomiting and diarrhea.

Participants in the study were diagnosed with cancer that had spread to bones, most often from prostate, breast and lung cancers. Median age was 65 years with 59% male patients and 41% female patients.

Overall median survival was eight months for both single-fraction treatment and multiple-fraction treatment patients.

Approximately 50 per cent of radiation treatments across all disease sites are for the purposes of symptom management for patients with advanced cancers.

The study was made possible through NCIC CTG's grant funding from the Canadian Cancer Society Research Institute. The NCIC CTG also receives grant funding support from the U.S. National Cancer Institute.

For more information, please contact: Ms. Natalie Chung-Sayers, (416) 480-4040, natalie.chung-sayers@sunnybrook.ca

An innovative self-care module for palliative care medical learners

By Hyon C. Kim, MD, MTS, CCFP, Elaine Rapp, MSW, RSW, Ashlinder Gill, PhD(c), and Jeff Myers, MD, MsEd, CCFP

This article is an excerpt from the Journal of Palliative Medicine, Volume 16, Number 6, 2013, Mary Ann Liebert, Inc. doi:10.1089/jpm.2012.0351

The physician-patient relationship is an essential element of a patient's overall care. Central to this relationship is the physician's ability to offer him/herself as a therapeutic instrument of healing. As such, self-care is not only necessary for the maintenance of a physician's well-being, but it also impacts the quality of care physicians are able to provide their patients. Ideally, development of skills such as self-reflection and self-awareness that enhance self-care should be integrated into a physician's daily practice. Physicians who are self-reflective and possess a high level of emotional self-awareness are best equipped to understand how their personal attitudes, values, and beliefs impact their behaviours toward other people. They are also better able to manage and overcome the stresses that arise in clinical practice.

Palliative care is a uniquely demanding field in that clinicians routinely address the complex needs of patients living with incurable illness. Due to their relative inexperience, medical learners completing a palliative care educational experience are

particularly vulnerable to the stresses that are often encountered. To address this educational need, a structured self-care module was developed for medical learners rotating through a palliative care clinical rotation.

Components of the self-care module include completion of a process recording exercise, a structured reflection, and participation in a facilitated group discussion. Process recording is a reliable and effective self-care educational tool used commonly in social work training. It involves transcribing a client interview, reflecting on the feelings and thoughts that arise during the interview, and sharing these elements with a field mentor or supervisor. Process recording is intended to provide learners with a structured opportunity to practice self-reflection and develop self-awareness within the context of a supportive relationship. In social work education, process recording is one of the best learning and teaching tools available. Within such a context it has been demonstrated that both self-reflection and self-awareness help learners enhance clinical competence, avoid boundary violations, and prevent burnout. These components are essential to the self-care and the development of the learner.

Learners were asked to interview one patient or family caregiver with whom they could spend at least 20 to 30 minutes,

discussing relevant palliative care issues including physical, psychosocial, and spiritual issues. To improve learners' comfort level around conversations of a spiritual or religious nature, they were given the HOPE acronym in the self-care module instructions. HOPE stands for H: sources of hope, strength, comfort, and meaning (What are the sources of hope for you at this time?), O: role of organized religion (How are these a source of support to you?), P: personal spirituality or practices (Are there any particular spiritual practices that give you meaning at this time?), and E: effects on medical care and end-of-life decisions (How would you like me to address some of these spiritual issues?).

Following the interview, learners were asked to write an accurate transcription of their conversation and complete four self-reflection questions: 1) What were the strengths and weaknesses of the interview?; 2) What feelings were shared by the patient during the interview?; 3) What were your thoughts and feelings during the interview?; and 4) What do you wish you could have said or done during the interview? After the transcription and self-reflection questions were completed, learners participated in a group discussion with other learners facilitated by a palliative care physician and a

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Can compassion fatigue?

By Mary L.S. Vachon, PhD, RN

Compassion fatigue has been described as the “natural consequent behaviours and emotions resulting from knowing about a traumatizing event experienced by a significant other—the stress resulting from helping, or wanting to help, a traumatized or suffering person”. The phenomenon is connected to the therapeutic relationship between the health care provider and patient. An individual’s capacity for empathy and ability to engage, or enter into a therapeutic relationship is central to compassion fatigue. Individuals who display high levels of empathy and empathic response to a patient’s pain, suffering or traumatic experience are more vulnerable to experiencing compassion fatigue.

Key elements within the compassion fatigue model include empathic ability, empathic response and residual compassion stress. The model is based on the assumption that empathy and emotional energy are the critical elements necessary

palliative care social worker. The purpose of this session was to give learners an opportunity to debrief on their experiences, to encourage honest discussions and to promote self-care through further self-reflection and deepening self-awareness.

Proceeding the facilitated group discussion, learners completed evaluations of the module. Eighty-six per cent of learners found the discussion to be helpful in reflecting on their clinical encounters, 86% gained an appreciation for the importance of self-reflection and self-awareness as a component of self-care, and 97% gained a greater appreciation for sharing clinical experiences with other learners.

This novel self-care module was found to be a well accepted, useful, and operationally feasible educational experience for postgraduate and undergraduate learners completing a palliative care educational experience. It enabled learners to appreciate the importance of self-reflection, self-awareness, and sharing clinical experiences with module facilitators and colleagues as important components of self-care.

For the full text article and a list of all references, please go to: <http://online.liebertpub.com/doi/pdfplus/10.1089/jpm.2012.0351>

to forming a therapeutic relationship and therapeutic response. While each factor is defined (e.g., empathic ability “is the aptitude of the psychotherapist to notice the pain of others”), there is limited description of how each factor potentially interacts with another.

Compassion satisfaction, compassion fatigue and burnout were studied in a national Canadian study of 630 hospice/palliative care staff. Nursing reported the highest level and administration reported the lowest level of compassion fatigue. Medicine and nursing had the highest levels of burnout.

The top three hospice/palliative care services provided were:

- Assistance with provision of relief from physical, emotional and/or spiritual pain or distress
- Providing psychosocial support to patients and/or families
- Providing emotional support to other team members.

Those providing each of these services reported higher levels of compassion fatigue and burnout and no significant difference in levels of compassion satisfaction compared to those who did not provide the service.

At the Odette Cancer Centre (OCC), Koo et al. did a study to discern the predisposing factors for occupational stress within the Rapid Response Radiotherapy Department (RRRP) and with RTs and RNs at OCC. Compassion fatigue was significantly higher in the RRRP team than in the nurses. Greater self-reported spirituality was predictive of higher compassion satisfaction—those reporting no or lower spirituality experienced higher levels of burnout.

Compassion fatigue is actually measuring factors involved with empathy. The two concepts are different. Compassion “can be described as having two main components: the affective feeling of caring for one who is suffering, and the motivation to relieve suffering”. “*The intention to transform suffering is one of the features that distinguish compassion from empathy* (italics not in original). From the point of view of compassion, intention is a key process in the cultivation of this mental process”. Compassion should be the basis of medical care.

“For clinicians, kindness and equanimity are essential affective processes associated with compassion. Kindness is characterized by a dispositional tenderness toward others combined with genuine concern. Equanimity is a process of stability or mental balance that is characterized by mental composure and an acceptance of the present moment. These two qualities are essential for clinicians who care for the dying.”

Gonzalez says that true compassion is deep caring without attachment. This is not the same as deep caring with detachment, which would imply an arm’s-length relationship that does not touch you, where you could not feel the pain or get hurt in the process of caring.” This compassion is caring deeply, but not being attached to the outcome. True compassion with non-attachment to outcome builds resilience and keeps us from burning out. Attachment refers to the unrelenting drive to succeed, to acquire, to compete, to control, and to the inability to let go.

Valent believes that so-called compassion fatigue arises from a failed survival strategy—from a rescue-caretaking response. He theorized that compassion fatigue occurs when one cannot rescue or save the individual from harm, and results in guilt and distress.

Equanimity is the ability to accept what is without resistance. Halifax says “Equanimity as well supports empathy, another affective feature frequently associated with the priming of compassion. Empathy is affective attunement with another. Affective attunement, often associated with compassion, might or might not elicit kindness, depending on the psychological makeup of the experiencer or the capacity of the experiencer to regulate her or his arousal level and maintain equanimity. In the case of the latter situation, emotion regulation and attentional and affective balance are essential. These conditions, when engaged, can lead to compassion.

True compassion cannot fatigue. However, true compassion requires self-compassion. The heart first pumps blood to itself.

For more information, please email: maryvachon@sympatico.ca

References

References available upon request

End-of-life care/les soins de fin de vie

By Philip C. Hébert, MD, PhD, Professor Emeritus, author of *Doing Right: A Practical Guide for Physicians and Medical Trainees*

In 1991, Quebec made Canadian medical history when a patient was allowed to refuse life-sustaining care. Nancy B., a 25-year-old woman, had been hospitalized since 1988 with an unusual and extremely severe form of Guillain-Barré syndrome (bedridden and hooked up to the ventilator every hour of every day). Her condition was considered incurable, but not “terminal”.

Nancy B. expressed a firm wish to be removed from the ventilator and be allowed to die—‘life was no longer livable’ for her. Her care providers, worried they might be charged with negligence or assisted suicide if they acquiesced to Ms B.’s request, took her case to court. This was not an unfounded concern. Section 215c of Canada’s *Criminal Code* requires care providers to provide the “necessaries of life” to a person under their charge “if that person (i) is unable, by reason of detention, age, illness, mental disorder or other cause, to withdraw himself from that charge, and (ii) is unable to provide himself with necessities of life.” Moreover, section 217 concerns “the duty of persons undertaking acts”: “Every one who undertakes to do an act is under a legal duty to do it if an omission to do the act is or may be dangerous to life.”

Together these sections suggested to some that stopping life-sustaining treatment of a patient who is dependent on others for care might be a crime.

The Quebec Superior Court ruled, however, that stopping treatment should be considered a matter of appropriate health care. “What Nancy B. is seeking,

relying on the principle of autonomy and her right of self-determination, is that the respiratory support treatment being given her cease, so that nature may take its course; that she be freed from slavery to a machine, as her life depends on it.” This, the Court recognized, would require the assistance of another person—her doctor—to remove the ventilator, and should not be considered a crime. The Court’s ruling solidified the right of capable adult patients to refuse any and all medical care.

In 2013, Quebec is making history again. The Parti Québécois has tabled Bill 52, “An Act respecting end-of-life care”. This Act allows for the compassionate accelerated death of irreversibly suffering terminally ill patients. Currently, federal law makes it a crime to help another person die. Canadian law does not recognize the category of compassionate assistance at death, instead treating it as murder.

Quebec proposes to take “assistance at death” of the terminally ill out of criminal law and put it where it better belongs, in the realm of health care, a provincial matter. We do already “assist” patients in their dying, of course—palliative care, for example, is meant to ease the passing away of patients and tolerates escalating doses of drugs, even at the risk of causing the earlier death of the patient. The difference comes down to motive and intent: the health care professional providing palliative care does not *aim* at the patient’s death. By contrast, the Quebec law would allow health professionals to take measures—such as

terminal sedation and active euthanasia—that *would* lead directly to the patient’s demise. But the Act does much more than that: briefly, it requires all institutions to have end-of-life care policies and adequate provision of palliative care, it requires an oversight body to which assisted deaths must be reported and will be monitored, and provides regulations regarding “medical aid in dying”. Patients must be of “full age”, have an advanced incurable condition and unmitigated suffering, have freely and capably chosen medical aid in dying and attested to this by the appropriate form, and all this must be documented and verified by an independent physician. The Act allows for health professionals a “conscientious objection” to participation clause.

Quebec’s Act may be alarming to some. They worry that it will result in health professionals under-treating terminally ill patients and improperly treating others. This need not be so. Evidence from other jurisdictions suggests that a well-regulated aid-in-dying scheme can appropriately restrict the use of this option. Quebec’s governing party has proposed an option for the desperately ill that a majority of Canadians have supported for years. The debate that will ensue will no doubt be a lively one. It should cause each of us to consider how we would want to be treated were we suffering and close to death.

The Act may be found at: <http://www.assnat.qc.ca/en/travaux-parlementaires/projets-loi/projet-loi-52-40-1.html>

Making best use of our hospice beds: Palliative performance scores and length of stay for patients admitted to residential hospice care

By Marissa Slaven, MD, Teri Crockford, RN, CNS, and Nisha Goel, McMaster University Division of Palliative Medicine

Although as many as 80% of people express a wish to die at home, in fact this occurs in only 20% to 30% of patients in Canada. Hospices offer patients a safe and comfortable alternative to dying in an acute care facility. Unfortunately, there are 9,100 deaths annually in Ontario, but only 283 hospice beds. Residential hospices often have waiting lists for their beds and an undocumented percentage of patients die waiting for a bed, resorting to acute care facilities when their care needs cannot be met at home. We hypothesized that inappropriate selection of patients for hospice admission (e.g., those with very prolonged lengths of stay [LOS] prior to death) may further limit hospice

bed availability. A better understanding of factors associated with prolonged LOS may facilitate better selection of patients for hospice. A Palliative Performance Score (PPS) of 40% or less (consistent with patients being mostly bed-bound) on assessment is required prior to hospice admission. Evaluation of this routinely measured metric and any association with LOS is of particular importance.

We reviewed 40 consecutive patients admitted to our community hospice over a six-month period to assess the relationship between PPS at different time points and LOS. All patients had PPS recorded on referral, on intake assessment, and again on hospice admission. Thereafter, it was

recorded on a weekly basis. Additional basic demographic information was collected including location of referral (home or acute care facility). Length of stay was calculated from hospice admission to the date of death or discharge. Pearson correlation coefficients (r) were used to evaluate the association between PPS measured at different time points. Given that length of stay (LOS) is not symmetric, Spearman r were used in lieu of the Pearson r to evaluate associations involving LOS. Linear regression was used to investigate whether PPS at time of referral, on assessment, or at time of hospice admission was associated with LOS.

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Unrealistic optimism in patients with advanced cancer

By Irene Ying, MD, MHS(Bioethics), CCFP, Division of Palliative Care, University of Toronto

This past June, a book called *Denial: Self-Deception, False Beliefs, and the Origins of the Human Mind* was published. Co-authored by Dr. Ajit Varki, physician and professor of cellular and molecular medicine at the University of California, San Diego, the premise of the book is that humans did not climb the evolutionary hierarchy due to any biological superiority, but rather due to our unparalleled ability to deny reality despite incontrovertible evidence. Although this theory is controversial, it underscores unrealistic optimism as a defining characteristic of the human psyche and helps to explain why some patients with advanced cancer may find it so difficult to accept the incurable nature of their disease.

“Unrealistic optimism (UO)” has been defined as when “a person believes that s/he is more likely to experience positive outcomes (or less likely to experience negative outcomes) than other similarly situated”. Congruent with Dr. Varki’s theory, UO has been linked to better psychological outcomes for advanced cancer patients. A 2001 study found that patients with metastatic renal cell carcinoma and metastatic melanoma who displayed *treatment-specific* optimism (such as the belief that chemotherapy would cure or halt progression of their cancer) were at a lower risk of depressive symptoms. A more recent study found that *the more patients misunderstood* their treatments to be potentially curative, the *higher* patients rated their physicians’ level of communication. This would indicate that optimism, even when unrealistic, confers psychological benefit and may enhance the physician-patient relationship. Then why do these patients’ inaccurate beliefs that a cure is possible need to be dispelled?

Although denial, including wilful ignorance of our own mortality, may have had its advantages when our ancestors faced

significant risks to procreate, Varki goes on to argue in his book that it has, in contemporary times, become a liability to our well-being. In patients with advanced cancer, denial of reality is problematic for a number of reasons. Patients who have overly optimistic outlooks are more likely to have undesired outcomes such as hospital readmissions, resuscitation attempts, or die while on ventilator support—all without any survival advantage.

Furthermore, the above studies, which imply psychological benefit from UO, are limited by their cross-sectional design and do not capture the decisional regret patients may feel when they realize at the eleventh hour that death is imminent. For example, patients may lament having not spent time with loved ones, or putting their affairs in order. And, as patients become weaker, their surrogate decision-makers are often left to infer what their loved ones would have wanted—which is no easy task. Studies examining surrogate decision-makers and families of patients in the ICU found PTSD levels of distress during and even six months after the hospital stay.

A patient’s persistent belief that their advanced cancer is curable is also ethically problematic in ways other than the inherent harm it may cause. First, it is questionable whether a patient can autonomously consent to chemotherapy or radiation if they do not understand the intention of the proposed treatment. Second, given that the fiduciary relationship between physician and patient is based on trust and truth-telling, physicians may feel torn between their duty to truthfully prognosticate and their desire to maintain the hopes of their patients. In fact, one American study found that physicians would only give a frank estimate of prognosis 37% of the time when a survival estimate was requested. And, lest we think that patients are the only ones affected by UO,

a systematic review found that physicians also consistently overestimate prognoses in patients with advanced cancer.

So, what can we, as health care providers, do to mitigate the harm from UO? The first goal of physicians should always be to attempt truthful prognostication while maintaining *general* optimism. Information should be clear without the use of euphemisms, jargon (e.g., remission), or over-reliance on statistics. Although we may see statistics as being objective and “safe”, a study involving women undergoing screening mammography found that a third of respondents thought 1,000 fair flips of a coin would result in less than 300 heads. This underscores the prevalence of innumeracy in the general population. A more useful approach may be to frame options in terms of values. For example, a patient may clearly articulate that quality of life or spending time with loved ones is more important than a small chance of improved survival.

Physicians must also be empathic to the process of truth acceptance and acknowledge that patients may be too overwhelmed initially to process information. Of course, concomitant psychiatric disorders such as depression should also be ruled out. Clinicians must also communicate with each other to ensure that the message across disciplines is consistent. Despite all this, there will always be a subset of patients who continue to believe their disease is curable. This may be an important adaptive mechanism for these patients, and perhaps our focus should not be on correcting this misunderstanding but, rather, to support the creation a “back-up plan”. Persistent unrealistic optimism is not mutually exclusive with the ability to take precautionary measures. In fact, the phrase “hope for the best, prepare for the worst” not only benefits patients with advanced cancer, but is a good rule of thumb for life in general.

Finally, we must acknowledge that UO is perpetuated not only on an individual level, but also on a societal level. We are seemingly inundated with stories in the media touting the latest medical breakthrough. André Picard, public health reporter for the *Globe and Mail*, recently cautioned against such hype tactics, reminding his colleagues “the language of science and medicine should be cautious and humble, because diseases like cancer are relentless and humbling.”

References

References available upon request

Making best use of our hospice beds

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In our sample, 30% of patients had an LOS less than one week and 55% stayed less than two weeks. However, 15% had an LOS greater than three months (95% CI 5.7%-29.8%). A higher admission PPS ($p=0.037$), being admitted from hospital/retirement home ($p=0.03$) and having no change between referral and admission PPS ($p=0.002$) were all associated with longer LOS. PPS on referral ($p=0.85$) or assessment ($p=0.71$) were not associated with LOS. Twenty patients with a decline in their PPS between referral and admission had a median length of stay of four (2 to 8.5) days, and only one (5.0%) stayed

for >90 days. In contrast, in 20 patients with no change or an improvement in their PPS from referral to admission, median LOS was 34 (11 to 90) days, and five (25.0%) stayed for >90 days. Of patients with a decrease in PPS between referral/assessment and assessment/admission, 14 (70%) had an LOS of <14 days, compared with only four (20%) of those with no decline.

Limited hospice resources may be most efficiently utilized for patients coming from home with a lower PPS score and evidence of declining PPS score in the interval prior to admission.

Continuing Medical Education 2013–2014

By Ewa Szumacher, MD, FRCP(C)

Continuing Medical Education (CME) can update health care professionals on the latest advances for modifications to their clinical practice. At the request of the CME organizers, *Hot Spot* will list the national and international CME activities in palliative medicine that are of interest to our readers. Please forward details of the CME activities to:

Ewa.Szumacher@sunnybrook.ca

- **October 10, 2013.** 2nd Annual Sunnybrook Education Conference: Digital Learning, Toronto, Ontario, Canada, Sunnybrook Health Sciences Centre. www.sunnybrook.ca/education
- **October 11–12, 2013.** 17th Annual Interdisciplinary Conference on Supportive Care, Hospice and Palliative Medicine (MD Anderson Cancer Center) (9th Annual Intensive Physician Board Review Course October 8–10, 2013), Houston, Texas, USA. www.mdanderson.org/education-and-research/education-and-training/schools-and-programs/cme-conference-management/conferences/postcard---17th-annual-palliative-save-the-date---final-2-22-13--2-.pdf
- **November 7–9, 2013.** Advanced Breast Cancer Second International Consensus Conference (ABC2), Centro de Congressos de Lisboa (Praça das Industrias), Lisbon, Portugal. www.abc-lisbon.org
- **November 8–9, 2013.** 2013 Best of ASTRO, Hilton San Diego Bayfront, San Diego. <https://www.astro.org/Meetings-and-Events/2013-Best-of-ASTRO/Index.aspx>
- **November 14–15, 2013.** IV International Workshop on the Treatment of Hepatic and Lung Metastases of Colorectal Carcinoma, Barcelona (Spain). www.oncology-bcn.com

- **November 15–17, 2013.** 5th European Multidisciplinary Meeting on Urological Cancers, Marseille, France. www.esmo.org/Conferences/EMUC-2013-Urological-Cancer
- **November 21–24, 2013.** AORTIC Conference 2013, Durban, South Africa. www.aortic2013.org
- **December 11–12, 2013.** 3rd International Gastrointestinal Cancers Conference 2013, Antalya, Turkey. www.esmo.org/Conferences/Oncology-Conferences-Calendar/3rd-International-Gastrointestinal-Cancers-Conference-2013
- **December 12–13, 2013.** XXI International Symposium TTD: Advances in the Treatment of Gastrointestinal Tumours, Cordoba, Spain. www.ttdgroup.org/ttd/index.html

2014

- **January 16–18, 2014.** 2014 Gastrointestinal Cancers Symposium (AGA Institute, ASCO, ASTRO & SSO), San Francisco, CA, USA. <http://gicasym.asco.org>
- **January 30–February 1, 2014.** 2014 Genitourinary Cancers Symposium (ASCO, ASTRO & SUO), San Francisco, CA USA. <http://gucasym.asco.org>
- **February 6–9, 2014.** GOG Semi-Annual Meeting, San Diego, CA USA. www.gog.org/meetinginformation.html
- **February 14–16, 2014.** Indian Association of Palliative Care 21st International Conference 2014, Kalinga Institute of Industrial Technology, Bhubaneswar, India. <http://iapcon2014.in>
- **February 18–19, 2014.** Sarcoma & GIST 2014, Milan, Italy. www.esmo.org/Conferences/Sarcoma-GIST-2014
- **February 20–22, 2014.** 2014 Multidisciplinary Head & Neck Cancer Symposium, JW Marriott Camelback Inn – Resort and Spa, Scottsdale, Arizona USA. <http://headandnecksymposium.org>

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Founders: Dr. L. Andersson, Dr. C. Danjoux

Editor: Dr. E. Chow

Associate Editor: Dr. C. Danjoux

Consultant: Dr. S. Wong

Advisers: Dr. E. Barnes, Dr. R. Goldman, Ms. L. Holden, Dr. A. Husain, Ms. N. Lauzon, Dr. L. Librach, Dr. A. Sahgal, Dr. E. Szumacher, Dr. M. Tsao

Editorial and Financial Manager: Ms. S. Yuen

Odette Cancer Centre, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, ON M4N 3M5
Tel: 416-480-4998, Fax: 416-480-6002

E-mail: stacy.yuen@sunnybrook.ca

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Myeloproliferative neoplasms—latest advances

HOT SPOT

Dr. Vikas Gupta, MD, FRCP, FRCPath, Associate Professor, Department of Medicine, Staff Physician, Leukemia/BMT Programs, The Princess Margaret Cancer Centre

The myeloproliferative neoplasms (MPNs) are a group of Philadelphia-negative (PH), or *BCR-ABL*-fusion gene-negative clonal stem cell disorders. These disorders include primary myelofibrosis (PMF), polycythemia vera (PV), essential thrombocythemia and myelofibrosis secondary to PV (PV-MF) and ET (ET-MF). The principal signs and symptoms of these disorders are cytopenias, splenomegaly, marrow fibrosis, and systemic symptoms due to elevated inflammatory cytokines. Patients with advanced MF can have decreased quality and quantity of life, similar to that of patients with other advanced malignancies. Some patients with MPNs transform to acute leukemia, which has an extremely poor prognosis.¹⁻³

Although allogeneic stem cell transplantation (ASCT) is curative, this treatment is applicable to only a minority of patients. Conventional therapies such as hydroxyurea, danazol, thalidomide and prednisone do not alter the natural history of the disease. Dysregulation of the JAK-STAT pathway is a hallmark of pathogenesis of MF. The discovery of the gain-of-function point mutation JAK2V617F in patients with

MPNs increased our understanding of the pathophysiology of PH-negative MPNs and led to the advent of new, specific therapeutic options. The first-in-class JAK1/2 inhibitor ruxolitinib was approved by Health Canada in 2012. With the wider availability of ruxolitinib and other novel therapeutic agents, the therapeutic landscape for MF is rapidly changing and is briefly reviewed here.³⁻⁵

Therapeutic options

Allogeneic stem cell transplantation (ASCT)

Although ASCT is the only curative treatment for MF, the significant morbidity and mortality resulting from it makes this procedure applicable to only 5% to 10% of patients. Major toxicities include graft failure and graft-versus-host disease. ASCT may be appropriate, however, for younger patients with good performance status without prohibitive comorbidities who have an expected survival of less than five years, are transfusion-dependent or are at increased risk of transformation to secondary AML. Progression-free survival of 40% to 50% at three years can be expected with ASCT.³

Conventional treatment

There is a wide array of conventional treatments available, aimed at palliating symptoms and improving quality of life. These revolve around reducing splenomegaly (the most common manifestation of MF), reversing anemia and resolving constitutional symptoms.

Splenomegaly

Hydroxyurea is the most frequently used drug for reducing spleen size and gives a 45% to 50% clinical improvement, but it can take up to three months to see

a response. Splenectomy has been shown effective in reducing transfusion dependence, pain and constitutional symptoms, but carries with it thrombosis, bleeding and sepsis that can occur in 25% of patients. Mortality can reach 10%. For patients in whom splenectomy is not appropriate (due to age or comorbidities) or are unresponsive to medication, splenic irradiation can be used. This can result in a reduction in spleen size and abdominal discomfort that can last three to six months. Unfortunately, splenic irradiation is accompanied by a high rate of severe cytopenias and increased transfusion dependence.³

Anemia

Anemia is a frequent symptom of MF and, along with transfusion dependence, is a poor prognostic factor in MF. Conventional treatments include epoietin alpha, androgens such as danazol, and immunomodulators such as thalidomide, used with or without

prednisone. Epoietin alpha, alone or in combination with interferon- α -2b and with or without GM-CSF, showed response rates of up to 60%. Female patients and patients with milder anemia appear to respond better. However, this treatment can result in progression of splenomegaly. The best patients to use epoietin alpha in are those with anemia and low erythropoietin levels. Thalidomide and related compounds have shown response rates of up to 30%, which can be improved with the concomitant use of prednisone. However, a large proportion of patients discontinue therapy due to adverse events such as neurotoxicity or myelosuppression.³

Constitutional symptoms

These symptoms include fatigue, weight loss, night sweats and pruritus and can have an impact on disease prognosis. However, conventional treatments are largely ineffective.³

Table 1: Tips on the use of ruxolitinib in routine clinical practice

1. Dosing should be individualized based on platelet count to maximize efficacy and minimize toxicities. In the COMFORT trials, the ruxolitinib doses were 15 mg BID for platelet counts of 100–200 x 10⁹/L, and 20 mg BID for platelet counts >200 x 10⁹/L. Start at 5 mg BID for platelet counts of 50–100 x 10⁹/L.
2. Ruxolitinib should be tapered slowly if treatment needs to be discontinued.
3. Educate patients about potential adverse drug effects while on treatment and during discontinuation.
4. Advise patients to maintain an adequate supply of drug at all times, e.g., going on vacation, etc. MF-related symptoms can return rapidly if the drug is discontinued abruptly.

Adapted from Gupta V, Foltz L, Sirhan S, et al.³



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Algorithm 1.				
	Low/Int-1 risk MF			
	↓	Careful evaluation of symptoms/investigations		
↓	↓		↓	
Asymptomatic/ low risk of LT*	Symptomatic/low risk of LT*		High risk of LT* or transfusion dependency	
<ul style="list-style-type: none"> Follow-up q 3-4 months Risk score assessment at each visit 	↓ Constitutional symptoms	↓ Splenomegaly	↓ HCT eligible	
	↓ JAK inhibitor therapy/clinical trial		↓ Yes	↓ No
			↓ Follow algorithm 2	↓ Clinical trial

Adapted from Gupta V, Hari P, Hoffman R. *Blood* 2012 Aug 16;120(7):1367-79.⁶
Int=intermediate; LT=leukemic transformation
* Risk of LT according to IWG-MRT criteria using cytogenetics, thrombocytopenia and PB blast %

Novel therapeutic options

JAK1/2 inhibitors constitute a major advance in the management of MF. The first of these, ruxolitinib, was recently approved by Health Canada under the brand name Jakavi® (known as Jakafi™ in the United States). Other JAK inhibitors are at various stages of clinical development, so, for the immediate future, ruxolitinib will be the most widely available agent in this class.³

Approval of ruxolitinib was based on the COMFORT-I and -II trials versus placebo and best available treatment (BAT), respectively, in patients with intermediate-2 or high-risk PMF, PV-MF or ET-MF. Significantly more patients in the ruxolitinib groups showed ≥ 35% reduction in spleen size than in either control group (42% vs. 0.7% and 28% versus 0% in the two studies respectively).³

Greater symptom improvement versus placebo was also seen in COMFORT-I and after a year of follow-up, there was increased mortality in the placebo arm. There was no survival difference between ruxolitinib and BAT in COMFORT-II.³

Ruxolitinib was generally well tolerated. Anemia, thrombocytopenia and neutropenia were the most frequent grade 3/4 hematologic adverse events. Dosage is determined by platelet counts (Table 1). The place in therapy of ruxolitinib is shown in Algorithms 1 and 2.³

Summary

MF is a rare but burdensome disease. Conventional therapies have not proven to be adequate treatment although, in the properly selected patients, ASCT can be curative. The discovery of the role of Janus

Algorithm 2				
	Int-2/High risk MF			
	↓ HCT eligible			
Yes		No		
↓ Establish goals of treatment		↓ Symptomatic disease		
↓ Curative	↓ Symptom control		↓ Yes	↓ No
↓ Consider BMT	↓	↓ JAK inhibitor therapy/ clinical trial	← ↓	↓ • Follow-up 2 months • Symptoms and risk score assessment at each visit

Adapted from Gupta V, Hari P, Hoffman R. *Blood* 2012 Aug 16;120(7):1367-79.⁶
Int=intermediate

Kinase in MF has resulted in the development of JAK1/2 inhibitors, most notably ruxolitinib, which is available in Canada. The decision-making regarding therapeutic options for MF can be challenging and these patients should ideally be managed on a shared care basis between the primary physician and a physician with expertise in management of MPNs. To improve the care and research efforts for MPNs, a nationwide coordinated and collaborative effort has been initiated by the recently formed Canadian MPN Group.

References

1. Tefferi A, Thiele J, Orazi A, et al. Proposals and rationale for revision of the World Health Organization diagnostic criteria for polycythemia vera, essential thrombocythemia, and primary myelofibrosis: recommendations from an ad hoc international expert panel. *Blood* 2007 Aug 15;110(4):1092-7.
2. Passamonti F, Maffioli M, Caramazza D, et al. Myeloproliferative neoplasms: from JAK2 mutations discovery to JAK2 inhibitor therapies. *Oncotarget* 2011 Jun;2(6):485-90.
3. Gupta V, Foltz L, Sirhan S, et al. Emerging therapeutic options for myelofibrosis: a Canadian perspective. *Am J Blood Res* 2012;2(3):170-86.
4. Harrison C, Kiladjan JJ, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. *N Engl J Med* 2012 Mar 1;366(9):787-98.
5. Hoffman R. Rational therapeutic options for patients with myeloproliferative neoplasms. *Trans Am Clin Climatol Assoc* 2011;122:11-26.
6. Gupta V, Hari P, Hoffman R. Allogeneic hematopoietic cell transplantation for myelofibrosis in the era of JAK inhibitors. *Blood* 2012 Aug 16;120(7):1367-79.