Breast cancer

SENTINEL NODE BIOPSY

Shailendra Verma, MD, FRCPC, FACP, Medical Oncologist, Ottawa Hospital Regional Cancer Centre; Associate Professor, Department of Medicine, University of Ottawa

STUDY SUMMARY: Impact of SN IHC-detected metastases on survival

Cote R, Giuliano AE, Hawes D et al. ACOSOG Z0010: A multicenter prognostic study of sentinel node (SN) and bone marrow (BM) micrometastases in women with clinical T1/T2 N0 M0 breast cancer. ASCO 2010, Abstract CRA 504.

In this prospective, multicentre study, sentinel nodes (SN) were identified in 5,184 of 5,485 pts (94.5%). Histologic SN metastases were found in 23.9% of patients and immunohistochemistry (IHC) detected an additional 10.5% positive SN. Bone marrow (BM) metastases were identified by IHC in a further 3%. The 5-year overall survival (OS) is summarized in Table 1. Involvement of SN detected by histology, but not by IHC, reduced OS significantly. BM IHC positivity significantly predicted decreased OS (p=0.015). The authors concluded that as the SN IHC-detected metastases appear to have no significant impact on OS, routine examination of SN by IHC should be reconsidered in this patient population.

<table>
<thead>
<tr>
<th>Group</th>
<th>% alive at 5 years (95% CI*)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SN histology status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>positive</td>
<td>92.8 (91.3 to 94.3)</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>95.6 (95.0 to 96.3)</td>
<td>0.0002</td>
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<tr>
<td>SN IHC status</td>
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<tr>
<td>positive</td>
<td>95.1 (92.7 to 97.5)</td>
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<tr>
<td>negative</td>
<td>95.8 (95.0 to 96.5)</td>
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</tr>
<tr>
<td>BM IHC status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>positive</td>
<td>90.2 (84.6 to 96.2)</td>
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</tr>
<tr>
<td>negative</td>
<td>95.1 (94.3 to 95.8)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*CI=confidence interval

STUDY SUMMARY: Sentinel node resection vs conventional axillary dissection

Krag DN, Anderson SJ, Julian TB et al. Primary outcome results of NSABP B-32, a randomized phase III clinical trial to compare sentinel node resection (SNR) to conventional axillary dissection (AD) in clinically node-negative breast cancer patients. ASCO 2010, Abstract LBA505.

In this large prospective randomized Phase III trial, 5,611 women with operable, clinically N0, invasive breast cancer were randomized to SNR + AD (Group 1) or to SNR alone, with AD only if SNs were positive (Group 2). The 3,989 (71.1%)...
SN-negative patients were followed for events, with followup information obtained for 99.9%: 1,975 in Group 1 and 2,011 in Group 2. Median time on study was 95.3 months. Comparisons of OS (Group 1 vs Group 2) yielded an unadjusted HR of 1.20 (p=0.12) and an adjusted hazard ratio (HR) of 1.19 (p=0.13). Five-year Kaplan-Meier estimates for OS are 96.4% in Group 1 and 95.0% in Group 2 and the 8-year estimates are 91.8% and 90.3%, respectively.

Comparisons of DFS (Group 1 vs. Group 2) yielded an unadjusted HR of 1.05 (p=0.54) and an adjusted HR of 1.07 (p=0.57). No substantial differences could be seen across sites for first treatment failure. Five-year Kaplan-Meier estimates for DFS are 89.0% in Group 1 and 88.6% in Group 2, and the 8-year estimates are 82.4% and 81.5%, respectively. No significant differences were observed in OS, DFS or regional control between the trial groups. The authors concluded that SNR without AD is a safe and effective method for regional node treatment of SN-negative breast cancer patients.

**STUDY SUMMARY:** Impact of axillary dissection in sentinel node-positive women

Giuliano AE, McCall IM, Beitsch PD et al. ACOSOG Z0011: A randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive sentinel node. ASCO 2010, Abstract CRA506.

Clinically node-negative breast cancer patients who underwent SNR and had one or two SN with metastases were randomized to AD or no further axillary-specific treatment. All patients were treated with lumpectomy and radiation. Of the patients enrolled, 446 patients were randomized to SNR alone (with a median of 2 lymph nodes removed) and 445 to SNR plus AD (with a median of 17 lymph nodes removed). In AD patients, 17.6% had 3 or more involved nodes compared to 5.0% of SNR patients (p<0.001). Median followup was 6.2 years. Table 2 shows lack of clinical benefit of AD for patients with limited nodal disease. The authors concluded that despite the belief that AD improves survival, no significant difference was recognized in SN-positive women.

**COMMENTARY:** When one thinks of practice-altering developments that have occurred over the past 30 years in the field of early-stage breast cancer management, one thinks of groundbreaking studies that have led to breast-conserving surgery, the recognition of the potential systemic nature of the disease, the need for a systemic approach resulting in the appropriate use of adjuvant endocrine therapy in hormon-sensitive disease, and more recently, the use of adjuvant trastuzumab in human epidermal growth factor receptor 2 (HER2) overexpressing disease. While the use of cytotoxic chemotherapy has also played a pivotal role, the overall benefit in important subsets such as hormone-receptor-positive, intermediate-grade disease is being questioned. It is now widely acknowledged that the net effects of these studies on quality of life and mortality reduction in women with early-stage breast cancer have been monumental.

The 3 studies summarized above are landmark achievements in their own right and collectively contribute to the “dos and don’ts” in the surgical management of women with breast cancer.

The first study, ACOSOG Z0010, was conceived after the observations of Cote et al and Mullenix et al suggested a negative prognostic impact of a positive SN or BM micro-metastases at diagnosis. In this study, 5485 patients with T1-T2 disease were enrolled to undergo SN biopsy and BM aspiration — truly a laudable achievement! Contrary to earlier observations, a positive SN (by IHC) did not have prognostic impact compared to negative SN and, as one might expect, a positive BM clearly had an impact on survival. Of note, only 3% of patients had a positive BM. In this era of molecular prognostication, it is clear that there are more appropriate techniques available to determine the overall relapse risk of an individual woman.

AD has long been the gold standard of the surgical management of women with operable breast cancer. This has in part been augmented by the observation that AD has also been associated with improved survival. The advent of the SN biopsy over a decade ago has truly revolutionized the nodal staging of early stage disease. Although until now there have been virtually no prospective data comparing the outcomes of a SN procedure alone to AD in clinically node-negative, SN-negative disease, it has become standard practice to not perform an AD in such circumstances. The
Breast cancer

RACIAL SURVIVAL DISPARITY

Joseph Ragaz, MD, FRCP, Medical Oncologist, Clinical Professor, Faculty of Medicine and School of Population and Public Health, University of British Columbia.

TRIAL SUMMARY: Impact of Biology and Socioeconomic Status on Outcome


An analysis of the Southwest Oncology Group (SWOG) adjuvant breast cancer trials (n=6,676) showed that African American (AA) patients compared to others had significantly worse survival rates. The Albain et al study examined the estrogen receptor-positive (ER+) S8814 Phase III trial, which randomized postmenopausal ER-positive patients between tamoxifen and tamoxifen plus cyclophosphamide + doxorubicin + fluorouracil (CAF), to determine if the level of ER-positivity or expression of genes within the 21-gene Recurrence Score (RS) assay analyzed by reverse transcriptase polymerase chain reaction (RT-PCR) method would provide insight into the frequently reported inferior survival of AA patients compared to others.

The S8814 data was analyzed for DFS and OS for AA vs other patient groups. Within the subset available for RS analysis of prognosis/prediction of CAF benefit, the outcomes of AA vs others were assessed overall, by ER level and by composite RS, and each of the genes was analyzed by RT-PCR of the RS.

Nine percent of the 1477 patients were AA, and they derived similar benefit from CAF as the others. However, outcomes were poorer: DFS was worse (5-year DFS 67% AA vs 79% others; adjusted HR 1.65, log rank p=0.073). While there was no significant difference by race in ER level by Allred IHC score or by RT-PCR for each of the 4 ER genes, all 5 genes in the proliferation group had higher gene expression by RT-PCR in AA vs others (p<0.05 for CCNB1, MKI17, MYBL2, BIRC5; p=0.051 for AURKA). While Cox regression models that adjusted for nodes, CAF and RS made a marginal impact on the DFS HR by race (1.60), the HR decreased substantially to 1.23 upon adjustment for proliferation.

The authors concluded that AA patients in ER+ early breast cancer trials have worse survival than others due largely to tumours with higher proliferation and not to differences in endocrine responsiveness.

COMMENTS: This study explores the possibility of breast cancer genetic markers determined by the 21-gene molecular signature having different distribution according to race: AAs enrolled on the SWOG adjuvant clinical trials have a significantly higher yield of proliferation genes (HR: 1.64, p=0.014), potentially responsible for a more aggressive behaviour. This would endow the tumours of AAs with worse tumour biology and inferior survival.

The novelty of this part of the study is the analysis restricted to ER+ cohorts, with multivariate analyses of 4 classes (“axis”) of breast cancer tumour biology genes as measured within the 21-gene assay (Oncotype Dx) RT-PCR: proliferation axis (5 genes), invasion axis (2 genes), Her2 subgroup (2 genes), and estrogen axis (4 genes). Of these, the genes of the...
proliferation axis were significantly overexpressed among AAs, by over 40% (mean of the 5 proliferation genes, \( p=0.004 \)).

These observations add to the ongoing debate of biologic markers as potentially independent of lower socioeconomic (SE) status, the principle known cause for worse outcome in AA women.

Multiple past studies have demonstrated statistically inferior survival among AAs, but the statistical difference often disappeared after controlling for SE and other prognostic factors at diagnosis. The consensus of most past studies investigating AAs is that SE inequities are pivotal factors influencing the outcome, more so than biology or genetics. Poor SE background in AAs results in substantially fewer mammograms obtained, higher-stage cancer at diagnosis, and less compliance with curative therapies.

**EVIDENCE FOR SOCIOECONOMIC STATUS AS AN IMPORTANT FACTOR IN OUTCOME**

Although race as a risk factor for breast cancer survival has been demonstrated, most studies have not analyzed race against other prognostic or demographic factors consistently as an independent factor.

Barcenas reported from the Medical College of Georgia tumour registry\(^7\) that, compared with white women, AA women were more likely to be younger and have later-stage disease at diagnosis. They were also less likely to have received hormonal therapy, although similar rates of radiation, surgery and chemotherapy were reported. AA women had a significantly poorer 5-year OS (45% vs 54% in white women, adjusted HR=1.35; 95% CI 1.12–1.63, \( p=0.0031 \)). The issue of SE status is also highlighted in the recent study of “underinsured” breast cancer patients.\(^2\) Being underinsured connotes low SE status. The study showed that even in this more homogenous low-income underinsured population, further adjustment for SE status erased the significance of race as the predominant adverse factor.

**BIOLOGY AS POTENTIALLY PREDOMINANT FACTOR FOR POORER OUTCOME IN AAS**

Barnholtz-Sloan et al,\(^6\) in one of the largest recent analyses of genetic association according to race, evaluated 3,748 women (of whom 1400 were AAs) adjusting for age, race and European ancestry. Twenty-nine single-nucleotide polymorphisms (SNPs) from genome-wide association studies were analyzed. While details are complex, several of the genetic markers were increased in AAs (HR=1.27, 95% CI 1.04–1.56), but several were increased only in white women (HR=1.30, 95% CI 1.15–1.46). Another set of genes was increased only among younger age women, regardless of race (HR=1.35, 95% CI 1.02–1.78).

These results highlight the need to conduct genome-wide association studies among racially different populations and at different ages, as genetic differences may exist and could be either the result, or an actual cause, of different biology.

Another recent report\(^7\) analyzing 786 patients showed that 54% of AA patients compared to 39% of Caucasian patients had ER-negative tumours (\( p<0.05 \)), suggesting that ER-negative status associated with higher aggressivity could be the biologic factor responsible for the difference. Indeed, when controlling in multivariate analysis for ER status, the 5-year OS was the same at 77% for both AAs and Caucasian patient groups (\( p=0.59 \)). Thus, while the ER expression as a more aggressive biologic entity was higher among AAs, the survival when controlling for ER status was the same.

**WHAT TO DO WITH THE RESULTS**

In view of these data, how do we interpret the conclusions of Albain et al? The AA patients and the rest of women enrolled on the reported SWOG study were part of a randomized trial, allocated to identical therapy, with all patients ER+ and all having a similar distribution of the known main prognostic factors, including the frequency of the Oncotype Dx 21-gene RS. Yet the proliferation axis genes, known for affecting tumour kinetics with resulting enhanced tumour aggressivity, were significantly overexpressed among AAs.

These data may not refute other data highlighting socioeconomic shortcomings as important factor. On the contrary, the data showing more aggressive potential in newly diagnosed AA women, who as a group are already socioeconomically disadvantaged, emphasize the need for more effective preventive and screening efforts.

Much as in any other population subsets with high-risk situations for breast cancer, the significantly increased expression of genes in the proliferation axis should alert us to offer more rather than less primary care to AA women, including education, screening and monitoring breast health, as a substantial dent in their survival could be made.

The Albain et al study also highlights the possibility that large-scale testing for molecular signatures may confirm these findings in a more robust sample, with expectations that other genes related to either the proliferation axis or other biologic markers may soon follow. These steps prom-
ise potential for more effective targeted therapy research. One challenge is to continue expanding prospective testing of tumour biology markers through molecular signatures in newly diagnosed patients on a large scale; the other is to act appropriately on the present findings, like those reported by Albain et al.

This should involve higher vigilance in monitoring all the high-risk population cohorts such as AA women. AAs may deserve more assertive steps, leading to higher frequency of mammograms, magnetic resonance imaging (MRI) and/or higher enrollment with chemoprevention interventions.

References

Prostate cancer

ROLE OF DENOSUMAB IN PREVENTING SKELETAL-RELATED EVENTS

Daniel Heng, MD, MPH, FRCP, Clinical Assistant Professor, University of Calgary; Medical Oncologist, Tom Baker Cancer Center, Calgary.

TRIAL SUMMARY: Denosumab delays time to first skeletal-related event
Fizazi K, Carducci MA, Smith MR et al. Randomized phase III trial of denosumab versus ZA in patients with bone metastases from castration-resistant prostate cancer. ASCO Abstract LBA4507.

This Phase III, randomized, double-blind trial compared the efficacy and safety of denosumab vs. zoledronic acid (ZA) in 1901 patients with metastatic castration-resistant prostate cancer (CRPC) patients with at least 1 bone metastasis, but no prior intravenous (IV) bisphosphonate use. Patients received either subcutaneous (SC) denosumab 120 mg and IV placebo (n=950), or SC placebo and IV ZA 4 mg (n=951) adjusted for creatinine clearance every 4 weeks. All patients were instructed to take supplemental calcium and vitamin D. The primary endpoint was time to first on-study skeletal-related event (SRE) (i.e. pathologic fracture, radiation or surgery to bone, or spinal cord compression).

Denosumab significantly delayed the time to first on-study SRE compared with ZA (HR 0.82; 95% CI: 0.71, 0.95; p=0.008.) The median time to first on-study SRE was 20.7 months denosumab vs 17.1 months ZA. Denosumab also significantly delayed the time to first and subsequent on-study SRE (multiple event analysis) (HR 0.82; 95% CI: 0.71, 0.94; p=0.004). Greater suppression of the bone turnover markers urinary N-telopeptide and bone-specific alkaline phosphatase occurred in denosumab patients compared with ZA (p<0.0001 for both). Overall, adverse event (AE) rates (97% each) and serious AEs (63% denosumab, 60% ZA) were similar. Hypocalcemia was reported in 13% and 6% of denosumab and ZA patients. Osteonecrosis of the jaw occurred in 22 (2.3%) denosumab compared with 12 (1.3%) ZA patients (p=0.09). Overall survival (HR 1.03; 95% CI: 0.91, 1.17; p=0.65) and time to cancer progression (HR 1.06; 95% CI: 0.95, 1.18; p=0.30) were similar between treatment arms. The authors concluded that denosumab demonstrated superiority over ZA in delaying or preventing SREs in patients with bone metastases from CRPC.

COMMENTARY: SREs can have a significant impact on patients with metastatic CRPC. Bisphosphonates have been employed in patients with bony metastases from prostate cancer, breast cancer and multiple myeloma because they demonstrate an improvement in time to first SRE. In prostate cancer, there is controversy in their use due to unanswered questions about the clinical significance of SREs, dosing schedule, and when best to employ bisphosphonates. This has led to non-uniform uptake of the use of ZA in prostate cancer in different regions of Canada.

Denosumab is a fully human monoclonal antibody against receptor activator of nuclear factor κB-ligand, which is important in cellular signalling in the balance between osteoclast and osteoblast activity. Potential advantages include SC administration and lack of need to adjust the dose in response to renal function, when compared to ZA.

It is important to know that although time to first SRE has become a common clinical trial endpoint, certain SREs are of greater significance than others. For example, bone metastases causing cord compression and pain are more important to prevent than bone metastases that cause an asymptomatic pathologic compression fracture. Thus, when

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interpreting this composite endpoint, it is important to know that the driver of statistical significance for this trial was the need for radiotherapy (20%) and fractures (14.7%).

The trial was not powered to look at the difference between the 2 treatment arms in terms of very important endpoints such as cord compression and death. It would have been helpful to have presented the data from both arms comparing the rates of cord compression, need for surgery, fracture rate and need for radiotherapy.

Despite the lack of need to dose denosumab in relation to renal function, renal dysfunction was precipitated in 14.7% of patients vs 16.2% of the patients treated with ZA. In additional, the incidence of osteonecrosis of the jaw was numerically higher (2.3%) in the denosumab group versus the ZA group (1.3%). This suggests that careful monitoring is still important and likely no different when compared to ZA.

Denosumab has met its non-inferiority primary endpoint and superiority secondary endpoint when compared to ZA. This is similar to previous findings in metastatic breast cancer to the bone. Submission to regulatory agencies is pending. Unanswered questions remain, such as cost-effectiveness and the true benefit to patients in terms of preventing important SREs in the face of the risk of osteonecrosis of the jaw and renal dysfunction. Because of the variable adoption rates of ZA from province to province, the uptake of denosumab into clinical practice will likely be uneven.

**Prostate cancer**

**ROLE OF RADIATION IN LOCALLY ADVANCED PROSTATE CANCER**

Alan So, MD, FRCSC, Urologist, Vancouver General Hospital; Assistant Professor, Department of Urologic Sciences, University of British Columbia; Research Scientist, Vancouver Prostate Centre, Vancouver General Hospital.

**TRIAL SUMMARY: Hormone therapy plus radiation**


This 10-year study assessed the effect of radiation therapy (RT) on OS when added to lifelong androgen deprivation therapy (ADT) in locally advanced prostate cancer. Patients with T3/T4 (1057) or T2, prostate-specific antigen (PSA) > 40 µg/L (119) or T2 PSA > 20 µg/L and Gleason ≥8 (25) and N0/NX, M0 prostate adenocarcinoma were randomized to lifelong ADT (bilateral orchiectomy or luteinizing hormone-releasing hormone [LHRH] agonist) with or without RT (65–69 Gy to prostate ± seminal vesicles with or without 45 Gy to pelvic nodes). The primary endpoint was OS. Between 1995 and 2005, 602 patients were randomized to ADT and 603 to ADT+RT. The median followup was 6.0 years. The addition of RT to ADT significantly reduced the risk of death (HR 0.77, 95% CI 0.61–0.98, p=0.033). The disease-specific survival HR was 0.57 (95% CI 0.41–0.81, p=0.001) favouring ADT+RT. The 10-year cumulative disease-specific death rates were estimated at 15% with ADT+RT vs 23% with ADT alone. The trial results indicate a substantial overall survival and disease-specific survival benefit for ADT+RT with no significant increase in toxicity. The authors concluded that combined-modality therapy (ADT+RT) should be the standard treatment approach.

**COMMENTARY: This Canadian-led study, conducted through the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG), shows for the first time a survival advantage with the combination of RT and ADT using LHRH in patients with locally advanced prostate cancer. The study enrolled 1205 patients, and although a majority of patients were clinical stage T3 or T4, 144 patients clinically staged T2 on digital rectal exam (DRE) were included in the analysis. Furthermore, over 80% of patients in each arm had a Gleason score ≤7.

During the 10-year period of the study, 26% of men in the ADT monootherapy arm died of prostate cancer, compared to only 10% of the combination ADT plus RT arm. This important study now offers a treatment alternative to ADT...**
monotherapy for these patients, which has been the traditional standard of care. The results of the Warde et al trial are similar to a Scandinavian study in which an antiandrogen, flutamide, was used in combination with RT in patients with locally advanced disease. These 2 studies now confirm the benefits of combination therapy in men with prostate cancer that appear to be locally advanced on DRE, without an increase in severe toxicities ($\geq$ Grade 3).

Some important issues are raised by this study. Would the survival advantage be greater if currently used radiation dosages were used (i.e. 74–78 Gy rather than 65–69 Gy)? In addition, the optimal length of hormone therapy is not known. Considering the growing evidence of the negative metabolic and cardiovascular effects of hormone therapy, the benefits of long-term hormone therapy must be tempered by the side effects of long-term androgen deprivation. Finally, given that >80% of patients were classified Gleason $\geq$7, would the survival advantage be observed in patients with high-grade tumours? The answer to this question may be addressed in a subgroup analysis of the patients with high-grade disease within this study.

### Oncology practice

**AMBULATORY INTRAVENOUS (IV) CHEMOTHERAPY**

Jennifer Wiernikowski, MN, NP-Adult, CON(C), Advanced Practice Nurse Hematology/Bone Marrow Transplant, Juravinski Hospital and Cancer Centre, Hamilton Health Sciences, President, Canadian Association of Nurses in Oncology/Association canadienne des infirmières en oncologie

**STUDY SUMMARY: Ambulatory IV chemotherapy: Hazards and safety improvement recommendations**

Green E, White R, Janes, K et al. Improving the safety of ambulatory intravenous chemotherapy in Canada, CANO 2010, Merck Lecture-ship Award Winning Abstract.

A 20-month interdisciplinary research project was funded by a number of cancer and safety agencies across Canada to identify safety issues in ambulatory IV chemotherapy in a wide range of environments and to formulate safety improvement recommendations.

This study comprised 3 phases: 1) a national survey of oncology care providers, 2) week-long ethnographic field studies in 6 cancer centres across Canada, and 3) in-depth analyses of identified safety issues. The survey was completed by 331 providers. Respondents reported 213 medication error incidents. Respondents reported 213 medication error incidents. The authors concluded that this cross-Canada collaborative research identified a number of safety hazards in ambulatory IV chemotherapy, many of which are directly related to oncology pharmacy and nursing practice.

**COMMENTARY:** This award-winning lectureship provided CANO/ACIO members with the first glimpse at the data from this important work. The study was initiated in response to a tragic medical error. On August 22, 2006, a patient was due to receive her continuous infusion of fluorouracil (5FU) for advanced nasopharyngeal cancer when a pump programming error resulted in an accelerated drug infusion. She died 22 days after the incident occurred, which contributed to hemodynamic collapse and multi-organ failure. This began a quest for the root causes that contributed to this tragic event. The objectives of this 3-phase study were to identify current practices for ordering, preparing, labelling, verifying and administering IV chemotherapy in Canada, to identify additional sources of risk in a variety of environments and to recommend strategies for risk reduction.

Phase I of the study consisted of a survey of oncology healthcare professionals: 331 responses were collated from 120 nurses, 154 pharmacists, 25 physicians, 23 pharmacy technicians and 9 described as “other.” Almost all (95.5%) respondents were aware of the 5FU incident. An additional 217 medication error incidents were disclosed by study participants.

### IN BRIEF

**Already Known**

- ADT monotherapy has been the standard of care for locally advanced prostate cancer.

**What this study showed**

- ADT + RT resulted in significant survival benefits without an increase in severe toxicities.

**Next steps**

- Subgroup analysis is required to determine the survival advantage when higher radiation dosages are used and in patients with high-grade tumours, and, to define the optimal length of hormone therapy.

**Reference**


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Phase II consisted of field studies and was carried out in 6 ambulatory chemotherapy centres across Canada. This phase provided the opportunity to map out the processes involved in the delivery of ambulatory chemotherapy and highlighted the extreme level of complexity and variability of current systems. For example, large-volume general-purpose infusion pump programming errors and labelling were examined. Typically chemotherapy arrives in the chemotherapy unit already mixed in solution and labelled. Often the label includes the name and amount of the drug and the amount of infusate in the bag but the nurse is left to calculate the rate of the infusion and program that into the pump. In the field studies, the need to complete this calculation at the point of care raised strong concerns. The simple addition of the rate of infusion to the drug label could be an important patient safety intervention.

The findings from the surveys and the field studies gave rise to Phase III, a comprehensive analysis of the various data sets from which to distill the final recommendations themed as: elastomeric infusers, preprinted orders and change orders, mixing and checking practices, and additional issues.

Although the researchers felt elastomeric infusers continue to be the best tool for continuous ambulatory infusions of chemotherapy, they recognized that these devices may contribute to medication delivery errors. The flow rate of elastomeric infusers can be affected by environmental factors such as heat, infusate viscosity and the height of the pump above the central venous access device. This is information not broadly understood by nurses and is therefore unlikely to be transmitted to patients as an important safety consideration. The infusers come in a variety of sizes for a variety of clinical uses and yet they look dangerously similar. Selecting the wrong device for the infusion was noted as a concern by the research team. The study determined that homecare nurses did not have (and could not be expected to have) in-depth knowledge about continuous chemotherapy infusion and

**IN BRIEF**

**Already Known**
- Administration of chemotherapy in the ambulatory setting is complex and the risk for error exists.
- Safety can be enhanced by simplifying and standardizing processes.

**What the Study Shows**
- An alarming number of incidents were disclosed by survey respondents.
- Priority review is required for elastomeric infusers, preprinted orders and change orders, and mixing and checking practices.

**Next Steps**
- Further investigation is required to fully understand safety issues in mixing and checking practices in chemotherapy administration.

required more support in order to safely support patients at home. The recommendations related to elastomeric infusers include a need for comprehensive education resources for nurses and patients about the factors that can affect flow rate. In order to prevent selection error, the labelling of each infuser should be distinct, and organizations should stock only the most commonly used ones and store them in separate locations to reduce the risk of selecting the wrong size. Cancer programs will be challenged by the findings to determine better ways of connecting oncology nursing staff to community nurses to share information and engage in mentorship activities and education to enhance patient safety.

The Institute for Safe Medication Practices has outlined a hierarchy of effective interventions to reduce the risk of medication errors. The least effective interventions are those that depend on human memory for best execution and do not counteract bad process design. Such interventions include training and education, rules and policies, and reminders/checklists and double-checks. Although these may be supportive in any cancer care environment, they are not likely to be reliable enough on their own to prevent error from occurring. At the top of the hierarchy are design-oriented interventions including simplification and standardization, automation, computerization and forcing functions built into the systems to further reduce the chance for error. Although medication errors in ambulatory chemotherapy settings have been shown to be low, aligning systems and processes to maximize the best possible process design can reduce risk even further.

The American Society of Clinical Oncology and the US Oncology Nursing Society have published a document outlining chemotherapy administration safety standards in response to a lack of national standards for safe chemotherapy administration, especially in the ambulatory setting. CANO/ACIO is completing a Canadian initiative focused on ensuring safe chemotherapy delivery for all cancer patients regardless of where they receive their care. It is imperative that we commit to finding a way to ensure that the risks of serious drug errors in the cancer care system are fully mitigated. This type of cooperative comprehensive examination of errors through the lens of human factors evaluation can have important and durable impacts on the systems within which we work. At the time of the incident in 2006 Dr. Anthony Fields, currently Vice President, Cancer Corridor, Alberta Health Services and Professor of Oncology at the University of Alberta, said that while we were not able to learn from the mistakes of others, we must ensure others learn from our mistakes. To do this will require that we all familiarize ourselves with the full set of recommendations from this study and advocate for necessary changes in our systems to enhance the safety of chemotherapy administration.

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Oncology practice

COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

Jennifer Stephens, RN, BSN, MA, OCN, Staff Nurse, Leukemia/Bone Marrow Transplant Unit, Vancouver General Hospital, Vancouver, BC, PhD in Nursing student, University of British Columbia

STUDY SUMMARY: CAM patient information needs
Lambert L K, Balneaves LG, & Truant T. Wading through water: Patients perspectives of seeking complementary and alternative medicine (CAM) information. CANO 2010, Abstract III-08-B.

While most Canadians with cancer use complementary and alternative medicine (CAM) during their cancer journey, little is known about CAM information-seeking behaviour. In this study, data from over 30 qualitative interviews with cancer patients with a range of cancer diagnoses were analyzed using thematic analysis. Study findings showed that in the absence of CAM discussions with conventional health professionals, individuals relied on lay resources, such as the Internet and their social network for CAM information. These individuals reported being overwhelmed and confused by the amount of CAM information available.

Patients were interested in determining what CAM options were appropriate as well as the potential for side effects and interactions with conventional cancer treatments. Many individuals preferred to receive evidence-based CAM information from health professionals such as oncologists, while others preferred anecdotal information from lay resources and fellow cancer survivors. The authors concluded that information and decision support strategies are needed to assist people with cancer to make informed decisions about the use of CAM.

COMMENTARY: Current research about the use of CAM therapies by oncology patients is limited despite the growing interest in this topic by the general population.1 The National Center for Complementary and Alternative Medicine (NCCAM) estimates that over a third of US adults use some form of CAM.2 The Complementary Medicine Education and Outcomes Program (CAMEO) affirms that a majority of oncology patients seek CAM information.3,4 In light of these data, it is critical that healthcare providers (HCPs) are prepared to discuss CAM options with their patients. At the minimum, providers should be aware of resources patients can access to obtain additional information that is evidence-based and promotes safe usage.

In the Lambert et al study, data gathered through 30 face-to-face qualitative interviews offers a cross-sectional, broad perspective on 2 groups of patients — patients recently diagnosed with cancer and patients already undergoing treatment. Male and female participants were evenly represented, and most were prostate or breast cancer patients. Thematic analysis, a method which focuses on identifying themes and patterns of behaviour, demonstrated that after diagnosis, there was an even split between patients seeking information about CAM from lay resources or from health care professionals.

Needs identified by patients seeking CAM information included finding out about specific CAM treatment modalities, and determining whether or not particular practices would be appropriate for their cancer diagnosis. Patients also expressed concern about the potential side effects and efficacy of CAM, and the interaction of CAM with allopathic treatments. Of those patients who asked their HCPs (e.g. oncologist, general practitioner [GP], nurse) about CAM, most wanted decision support. Patients also relied on lay resources such as the Internet, books, family, friends, health store clerks and homeopathic physicians. The study does not indicate what percentage of patients sought information outside the allopathic context, so it is unclear if patients consulted both, or only one, of these information resources. What was obvious to the researchers is the constant struggle patients experienced around the credibility of CAM data, which presumably limits usage.

The definition of CAM is constantly under transition, blurring the understanding of what constitutes “complementary and alternative medicine.” It is unclear if patients in this study were asked to define CAM prior to their interview. Despite a growing social awareness and acceptance of CAM, a qualitative research pitfall (i.e. lack of predetermined

IN BRIEF

Already known
• Most Canadians with cancer use CAM during their cancer journey, but little is known about their CAM information-seeking behaviour.

What this survey showed
• Cancer patients want information about CAM, including treatment options, side effects, efficacy and the interaction of CAM with allopathic treatments.
• Many cancer patients rely on HCPs as well as lay resources to obtain information about CAM.

Next steps
• Further research must take into consideration patient awareness/use of CAM before the cancer diagnosis, and the impact of this information on CAM information-seeking behaviour and usage.
definition of CAM) may have impacted on the research findings. Further research should incorporate patient awareness and use of CAM therapies before the cancer diagnosis, and the impact of this pre-existing information on behaviour and choices related to CAM. Ongoing research by the CAM team and other international centres will continue to examine the role of CAM in cancer care, while framing how nursing and other HCPs can best serve patient needs.

References
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ONLINE RESOURCES FOR CHILDREN

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STUDY SUMMARY: Resources to support children who have parents with cancer

The study assessed an award-winning website developed by an interdisciplinary team (including clinicians and multimedia design experts) for children aged 6–12 years who have a parent diagnosed with cancer. The website was based on cancer literature addressing the impact of parental diagnosis of cancer as well as the learning characteristics, cognitive developmental level and the “digital behaviour” of the target audience and was tested by children, parents and clinicians during its development. The website integrates psychosocial and medical aspects of care by helping children explore nonverbal ways of expressing feelings and by providing basic information about cancer and its treatment. In the first month it was launched, there were 1256 visits to the site. In addition to being a useful resource for children, the site provides support for parents, school personnel and clinicians.

COMMENTARY: At the recent International Psycho-Oncology Society (IPOS) 12th World Congress in Quebec City, MacKenzie and colleagues presented an interactive website for families, clinicians and educators, designed to support children when a parent has cancer. Their presentation of the relevance of implementing novel approaches to address the role of CAM in cancer care, while framing how nursing and other HCPs can best serve patient needs.

At the Tom Baker Cancer Centre (TBCC) in Calgary, we offer a 5-week group support and education program for children and adolescents whose parents have cancer. The TBCC Kids/Teens Can Cope (KCC/TCC) program has been operating out of the Department of Psychosocial Resources since 1990. In recent years, our program enrollment has fluctuated. We conducted an environmental scan of group programs currently offered by Canadian cancer institutions for children and adolescents whose parents have cancer. Findings were presented at the IPOS 12th World Congress. We contacted the supportive care/social work departments of all major publicly-funded Canadian cancer care institutions via email or telephone. An interview was then conducted with a program facilitator, or clinician most knowledgeable of such programs offered at their institution. We found that one-third of Canadian cancer centres run such programs. Based on facilitator observation and informal feedback from participants, programs appear to be meeting a need for families who participate, however most programs are currently struggling with enrollment. Facilitators have varied their program structure by, for example, moving to a single afternoon format (vs after-school weekly) in an attempt to increase accrual. Videoconferencing was being used in one
centre to encourage participation for those who live outside of the city. The optimal format for providing children and adolescents with group support and education is not yet evident.

An important question is how to provide children and families the support they need, taking into consideration practical barriers which limit accrual to group support programs for children, including: greater financial and time strain associated with participating (e.g. travelling through congested cities); ensuring families in rural communities have access to services; maintaining after-school routines to not disrupt extracurricular activities; and a reluctance to participate in face-to-face groups due to anxiety or privacy concerns.

Online support groups may be a valuable intervention modality. A recent evaluation of the use and content of Web-based peer support in children coping with parental cancer demonstrated that Web-based support is an easy and accessible option. Internet-based modalities address the issue of practical limitations, allow parents to maintain after-school routines and thus a sense of normalcy for their children, are less intimidating than support groups, and are accessible to families in rural communities. Children and parents may initially prefer to explore the comfortable and fun avenue of an interactive website. In sum, MacKenzie and colleagues’ interactive website addresses a gap in supporting families who do not have access to or feel comfortable with support groups, or families who are who are quite resilient but would benefit from information and an avenue to enhance communication about cancer.

While there are many advantages of an interactive Website and other Internet/print resources, there are also disadvantages. The most notable disadvantage is that children are not able to benefit from interacting with others in a group format. A key element of group interventions is support: children connect with others who are in a similar situation and realize that they are not alone. Children may also benefit from hearing about how others cope with their fears, difficult emotions and changes within the family.

At the IPOS 12th World Congress, 4 other papers/posters and a workshop focused on the impact of parental cancer, and available resources for professionals and families in supporting children. Warnick conducted a workshop to review the current body of research and to provide strategies and resources to support children when a family member has cancer. McGoldrick and colleagues presented on the use of an animated television program that may be viewed by families in order to assist children to talk about their feelings. Moore and colleagues reported on the development of a new measurement instrument to identify parents’ concerns about their children when a parent has cancer. The 14-item Parenting Concerns Questionnaire (PCQ) contains 3 subscales: practical impact of the illness on child, emotional impact of the illness, and concerns about the co-parent. The PCQ demonstrated good psychometric properties, and correlated in expected directions with standardized measures of patient emotional distress and psychologic functioning. Higher PCQ scores were also associated with female gender, recent diagnosis, severity of disease and mental health comorbidity. This tool may help identify families that could benefit most from targeted intervention.

Psychosocial oncologists have shown considerable interest in identifying and reaching families who may benefit from support, and delivering timely and effective interventions when a patient has cancer. Group interventions and online resources for children and parents may play a preventive role in minimizing negative effects of parental cancer and in building resilience. Qualitative and quantitative research is needed to evaluate the effectiveness of interventions for children and families in their various formats. While Internet-based resources are not “therapy” per se, they can be therapeutic, and may fill a need for families who are not able to access or who do not need more intensive psychosocial support. Group interventions and online therapeutic resources should be promoted to families depending on particular circumstances and level of need.

The CancerCare Manitoba website has information about how children should be told that a family member has cancer and how to support children when a family member has cancer: www.cancercare.mb.ca/home/patients_and_family/patient_and_family_support_services/the_emotional_side_of_cancer/what_about_family_and_friends/talking_to_your_children/

References
For women with breast cancer, psychologic and physiologic risk is associated with restrained or dysregulated affect expression. This study analyzed coded emotional expression during group therapy sessions with the objective of testing whether greater fear, anger and sadness over time is related to a decrease in symptoms of trauma and depression. The method used involved coding a woman’s speaking time in 16 sessions per woman (N=37 women with usable video) for their first year in supportive-expressive group therapy sessions for families with a parent with cancer. Psycho-oncology 2009.

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Supportive-expressive group therapy (SEGT) is an intervention that explicitly encourages emotional expression, building social support and the examination of existential concerns. SEGT has been shown to improve coping and reduce mood disturbance and trauma symptoms, and in metastatic breast cancer patients. SEGT has also been shown efficacious in helping treat and prevent depression in patients with advanced cancer and to increase social functioning in this population. An attempt to demonstrate movement and content. The mean duration of a moment of 23 specifically coded affects were divided into 4 summary categories: primary negative, positive, constrained anger, and defensive-hostile affect. Change measured over time for each summary category served as independent variables predicting the slope of trauma and depression symptoms. The study results demonstrate that when the slope of primary affect increased over the year, there was a decrease in trauma symptoms. In contrast, when the slope of constrained anger increased over one year, trauma symptoms also increased. The author concluded that expressing vulnerable emotions in group therapy may allow breast cancer patients to more effectively process their distress, and if these emotions are expressed for long enough, other group members can intervene and respond, and active plans to relieve distress may result. Constraining anger resulted in increased symptoms of trauma over time.

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effectiveness of a brief version of SEGT for primary breast cancer patients was not successful.3

Some of the intriguing aspects of Geise-Davis’ study are that it uses a novel method of tracking and measuring emotional expression that is not reliant on self-report, and provides a means to examine processes of change over time.5

The study results provide evidence about mechanisms of change operating within SEGT that can be directly referenced to the theoretical basis of the intervention and thus allows us to peer into the “black box” linking intervention and outcome. The results should encourage group therapists utilizing SEGT to trust that their efforts to encourage and support patients in exploring emotionally challenging material through the expression of associated primary affect is grounded in a validated therapeutic approach with strong coherence between theory and evidence.

The methods developed and utilized by Geise-Davis represent an exciting and novel approach to inquiry that is suitable for exploratory research, as well as the empirical testing of hypotheses derived from theories of emotion regulation and processing. They constitute a valuable contribution to the methodologic foundations of a maturing discipline.

References


Disclosure statement:
Dr Specia is a successful co-applicant with Dr. Giese-Davis on a current research grant from the Canadian Breast Cancer Research Alliance entitled: A Multi-Site Randomized Control Trial Testing Efficacy of Professional and Peer-Led Online Support Groups for Young Canadian Breast Cancer Survivors.
**IN BRIEF**

**Already known**

- Cancer patients require ongoing symptom management advice and support.

**What this survey showed**

- Senior oncology nurses working in ambulatory settings provide remote support mainly via the telephone.
- Oncology nurses are generally confident in their ability to respond to common symptoms and they value symptom management protocols and guidelines.

**Next steps**

- Further development of clinical guidelines is needed to deal with the most common symptoms patients ask nurses about, as well as the symptoms nurses report the least confidence in addressing with patients.
- A better understanding of the processes by which oncology nurses provide remote support would be useful.

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**References**


**Disclosure**

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