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What is New in Supportive Care in Cancer?

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ABSTRACT The Annual Symposium of the Multinational Association of Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO) was held in Vancouver, Canada, June 24-26, 2010. The symposium brought together health care professionals from many countries and many fields of expertise for an excellent forum of ideas, lectures and collegial interactions, and discussed methods to minimize cancer-induced side effects, the symptoms and complications of its treatment, and psychosocial issues facing cancer patients and their families. Some ideas and studies selected from the presentations of different fields of supportive care in cancer presented in this symposium are introduced in this paper.

KEY WORDS: supportive care, MASCC Symposium, presentation.

Antiemetics

The NK1 antagonist aprepitant improves antiemetic efficacy in patients receiving carboplatin, oxaliplatin and cisplatin has been shown in a prospective randomized clinical phase III trail

Four randomized trials including 1872 patients receiving platinum agents was conducted by Dr. Richard J. Gralla, et al. Each trial had a control arm and an investigative arm adding the NK1 antagonist. In all trials the control arm on Day 1 was ondansetron + dexamethasone. Investigative arm added aprepitant 125 mg day 1, 80 mg on days 2 and 3. Control arms for delayed emesis with cisplatin: dexamethasone 8 mg bid in two studies; ondansetron 8 mg bid added in the third; in the aprepitant arm only 8 mg of dexamethasone daily was given. For delayed emesis in patients receiving carboplatin or oxaliplatin on the control arm, ondansetron 8 mg bid was given versus the aprepitant on the investigative arm. Three hundred and forty-five patients receiving carboplatin or oxaliplatin were randomized in the fourth study.

Odds ratios in the carboplatin or oxaliplatin trial and in the cisplatin meta-analysis are in Table 1. Odds ratios show similar magnitude of effect with carboplatin and cisplatin; absolute benefit is greater with cisplatin. Benefit occurs with aprepitant in patients receiving oxaliplatin, but the magnitude is less than that with the other platinum drugs.

Table 1. The results of meta-analysis of the oddsratios in carboplatin, cisplatin and oxaliplatin.

Agent	*n*	5-day no emesis OR	95% CI	*P*
Carboplatin	192	2.30	1.15, 4.63	0.019
Cisplatin	1527	2.38	1.92, 2.93	< 0.0001
Oxaliplatin	153	1.45	0.71, 3.34	0.274

Benefit is observed with the addition of aprepitant to antiemetic regimen for all 3 platinum agents. Analysis of demographic subgroups may suggest where control is greatest with aprepitant in patients receiving oxaliplatin. These results support broader use of NK1 antagonists in patients receiving platinum agents.

Role of ganaton in antiemetic therapy

Dr. Luidmila Manzyuk's study included 30 patients with a mean age-56 of years, with various malignant tumors. The chemotherapy included: ELF, FAC, FOLFIRI, PC, EP. Ganaton (G.) was used in 50 mg tablets. The doses and duration were as follows: on day 0, G. 50mg in the evening. On day 1 or from day 1 to 3 (depending on the regimen): G. 50 mg in the morning and a second 50 mg dose in 6 h after chemotherapy (CT), at daily dose of 100 mg. Thirty minutes before CT, 8 mg of Ondansetron (Ond.) was iv, and EP regimen, 16 mg of Ond. plus 8 mg of dex. After the CT, on Day 2 or Day 4, depending on the regimen, patients received 8 mg of Ond. Orally, plus 50 mg of G. 3 times a day at daily dose of 150 mg, were administered. The following 4 days, patients carried on with G. intake at 150 mg a day. For evaluation, the effect of G. was assessed as follows: "complete effect"—absence of vomiting and/or nausea on the days of treatment and in 24 h after CT, "partial effect"—mild nausea and/or 1-2 episodes of vomiting still remain, and "without effect". The evaluation of G. effect in prophylaxis delayed nausea was assessed as follows: "complete effect"—absence of nausea for 4 days after CT, and "without effect"—nausea still remained during the following days of observation.

The results of the study showed that the efficiency of G. plus Ond in prophylaxis of acute vomiting was 100%, and in prophylaxis of acute nausea—90% complete effect and 10% partial effect. Ganaton efficiency in prophylaxis of delayed nausea was 80% complete effect, and 20% of patients "without effect" or maintained mild nausea. Ganaton intake didn't cause any adverse reaction.

Control of nausea will require management of a range of physical symptoms and anxiety

A study led by Dr. Ian Olver demonstrated that the symptoms which the patients associated with nausea were vomiting, dry retching, loss of appetite, dizziness, and indigestion. Most patients described psychological symptoms. Some described a physical restlessness or a mental restlessness and inability to concentrate, with an underlying anxiety and negative emotion which could trigger nausea. Other triggers for nausea were odors, foods (particularly meat), changing posture, and brushing teeth. Nausea improved by avoiding triggers, eating light foods (often dairy, fruit, soft drink), and using antiemetics and hot-packs. A strong component in avoiding nausea was calming anxiety through relaxation, meditation, hearing reassurance that it passes, and using sedatives to induce sleep, and particularly distractions (movies, hobbies, excursions). Patients could distinguish chemotherapy-induced nausea from that associated with pregnancy or food and alcohol by its persistence and associated symptoms, particularly lethargy. It reminded them of their cancer diagnosis. Therefore, control of nausea will require management of a range of physical symptoms and anxiety.

Bone Complications/Cachexia

Subcutaneous denosumab was superior to zoledronic acid in delaying or preventing skeletal-related events across a broad cancer population with bone metastases

In a meta-analysis from 2 randomized, double-blind studies led by Dr. Allan Lipton, 2 pivotal trials, identically designed and analyzed, compared the RANKL inhibitor denosumab with zoledronic acid (ZA) in delaying or preventing skeletal-related events (SRE) inpatients with bone metastases. One trial included patients with breast cancer (n = 2046); the other, patients with advanced cancer (except breast or prostate cancer) or multiple myeloma (n = 1776).

This meta-analysis evaluated the effects of denosumab treatment on time to first on-study SRE (primary endpoint, non-inferiority, [synthesis method]; secondary endpoint, superiority [proportional hazards model]) and time to first and subsequent SRE (secondary endpoint, superiority [Andersn-Gill approach]). Every 4 weeks, patients received a fixed dose of subcutaneous denosumab 120 mg or intravenous ZA 4 mg adjusted for creatinine clearance.

The results of the study demonstrated that Denosumab was superior to ZA and delayed the time to first on-study SRE by 17% compared with ZA (HR 0.83; 95% CI: 0.74, 0.92; $P < 0.0001$ for non-inferiority; $P = 0.0008$ for superiority). Median time to first on-study SRE was 21.1 months for ZA and was not reached for denosumab. Denosumab also delayed the time to first and subsequent on-study SRE by 18% compared with ZA (multiple event analysis) (rate ratio 0.82; 95% CI: 0.74, 0.91; $P = 0.0003$). Denosumab reduced the mean skeletal morbidity rate (SREs/patient/year) *vs.* ZA (0.64 *vs.* 0.80; $P = 0.0006$). Both groups had comparable disease progression (HR 1.00; 95% CI: 0.92, 1.08; $P = 1.08$; $P = 0.90$), survival (HR 0.95; 95% CI:0.86, 1.05;

$P = 0.35$), adverse events (AEs; 96% denosumab, 97% ZA), and serious AEs (53% denosumab, 56% ZA). ZA-treated patients had increased rates of AEs potentially associated with renal toxicity (6.5% denosumab, 9.6% ZA). Incidence of osteonecrosis of the jaw was low and not statistically significantly different: 1.6% denosumab, 1.3% ZA. Therefore, subcutaneous denosumab was superior to ZA in delaying or preventing SRE across a broad cancer population with bone metastases.

The predictive value of serologic bone markers for the development of osteonecrosis of the jaw in patients receiving bisphosphonates (BPs)

In a prospective investigation conducted by Dr. Noam Yarom, data on demographics, comorbidities and BP treatment were collected on 78 patients scheduled for dento-alveolar surgery. Fifty one patients were treated with oral BPs for osteoporosis and 27 patients were treated with intravenous (IV) infusions of BPs for multiple myeloma or bone metastases of solid tumors.

Blood samples for c-terminal telopeptide of collagen I (CTX), bone-specific alkaline phosphatase (BAP) and parathyroid hormone (PTH) were taken preoperatively. Surgery was performed conservatively and antibiotic medications were prescribed for 7 days. Dento-alveolar surgery was performed on patients receiving IV BPs only when it was unavoidable.

The results showed that 4 patients on oral BPs (7.8%) and 14 on IV BPs (51.8%) developed bisphosphonate-related osteonecrosis of the jaw (BRONJ). CTX levels < 150 pg/mL were significantly associated with BRONJ development, with an increased odds ratio of 5.268 ($P = 0.004$). BAP levels were significantly lower in patients on oral BPs who developed BRONJ. PTH levels were similar in patients who developed BRONJ and those who did not.

In conclusion, the incidence of BRONJ following dento-alveolar surgery is higher among patients receiving IV BPs compared to patients on oral BPs. Measurement of serum levels of CTX prior to the performance of such procedures may be an important contribution to the risk assessment of subsequent BRONJ development.

Communication and Decision-Making

Factors influencing treatment choices in patients with newly diagnosed breast cancer

Dr. Dennis Citrin and his colleagues interviewed 30 women who delayed seeking a diagnosis or refused recommended conventional treatment in favor of alternative therapies ("refusers"); interviews were also conducted with 30 control subjects, who accepted both conventional and alternative treatment from the outset. Each woman completed the Beck Anxiety Inventory and the Rotter Locus of Control Scale[1] to identify differences in generalized anxiety and perceived locus of control. The results of the interviews demonstrated that fear and negative experiences with doctors were the main factors that caused women to reject potential life-prolonging conventional therapy. Refusers believed chemotherapy and radiotherapy were riskier and less beneficial than did controls ($P = 0.007$). Controls perceived alternative medicine alone as riskier than did refusers because its value for treating cancer is unproven ($P < 0.0001$). From their own research after diagnosis, refusers (but not controls) concluded that they could heal themselves naturally from cancer with even simple holistic treatments like raw fruits, vegetables, juicing and supplements. It is concluded that some women reject conventional breast cancer treatment, opting for alternative regimens alone despite physician warnings that this could cost them their lives. This decision is apparently due to a combination of fear, despair, negative experiences with doctors, and misinformation. According to these women, a caring, compassionate approach to cancer care and physicians who acknowledge their fears, communicating hope and encouragement, and educating them about their options would have led them to make better treatment choices.

A technical solution to improving hospice and palliative care

A user-friendly, EMR-compatible, software prototype that allows typical clinical data (blood pressure, disease, patient medical history, medications) and Patient Report Outcomes (PRO) to be entered and stored. This data is immediately available during the clinical encounter with graphically depicted summaries for patient history and PRO assessments, a trending feature that links symptom behavior to interventions, and ELVIS (a digital drawing tool for disease-based communication with patients/caregivers).

A user-centered design approach allowed for iterative cycles of needs/usability feedback from providers and patients/caregivers to be incorporated into the prototype's structure and features. To determine the needs and initial usability of the project's prototype, Dr. Niina Haas and her colleagues interviewed 8 providers and 18 patients/caregivers. Another usability test, consisting of patients/caregivers ($n = 18$) and provider ($n = 9$) interviews, assessed the functional prototype's design, usability, and usefulness.

The results of the interview showed that patients/caregivers ($n = 18$) reported that the prototype was usable (100%). It would facilitate patient-provider communication, shared decision-making, and self-management (100%). They would be willing to try the system and recommend it to their providers (100%). The providers ($n = 9$) felt that the prototype encouraged better: use of patient assessments in decision-making and patient care (100%), identification of cause/temporal relationship between care events and outcomes (100%), monitoring of patient status (100%), communication in a multi-

disciplinary team (100%), and operational efficiency and patient care quality (88.9%).

Dr. Haas concluded that quality of patient care and operational efficiency can be improved with an effective assessment, evaluation, and communication tool. This project developed such a tool.

Complementary and Alternative Medicine

Complementary medication-anticancer therapy interactions

A study to measure the prevalence of complementary medication use in patients receiving anticancer therapy (chemotherapy+/- radiotherapy) and identify the potential complementary medication-anticancer therapy interactions has been completed by Dr. Greeta Sandhu, et al. In her study, routine medication reconciliation was conducted over a month by the ambulatory cancer pharmacist in all new patients receiving anticancer therapy in the day therapy unit. Complementary and alternative medicines (CAMs) with the possibility to interact with anticancer therapies were identified using evidence based reference sources (e.g. Natural Medicines Database and Sloan-Kettering Cancer Center's herbal information website). Patients were advised on an appropriate course of action according to any identified interactions.

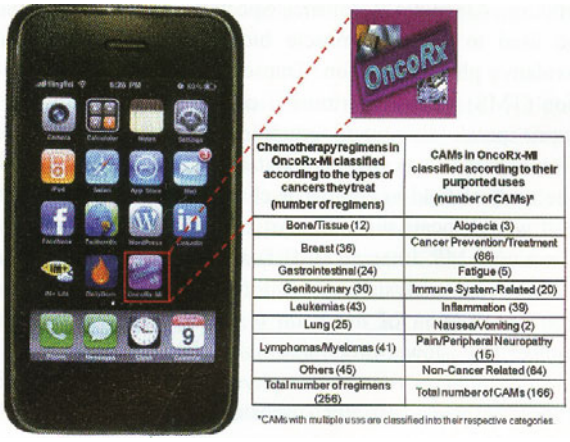
Fifty-seven percent of patients reported usage of CAMs (n = 32). The majority of the CAM users were being treated for solid malignant tumors (87%). Nearly all CAMs reported being used contained the potential to interact with the anticancer therapy (92%). Of these, 91% of the CAMs were successfully ceased by the ambulatory care cancer pharmacist on the initiation of anticancer therapy. The most common interactions were with CAMs that have activity that reduces free radical oxygenated species formation, inhibits platelet aggregation and induces/inhibits cytochrome P450 enzymes.

The results from this research demonstrated prevalence of CAM usage was over double in cancer patients than previous Australian studies. Medication reconciliation was valuable in determining CAM-anticancer therapy interactions. Highlighting the significance of the interaction to clinicians and modifying CAM usage accordingly in the patients has the potential to reduce risk that may occur when combining CAM and anticancer therapy.

Transcending chemotherapy regimen interactions with complementary and alternative medicine through 3G networks: Oncorx-Mi for the mobile internet (mobile internet)

Dr. Kevin Yap, et al. developed OncoRx-Mi, a first oncology-specific iphone application for single-and multiple-agent combination chemotherapy regimens (CRegs). In their procedures, data regarding anticancer drugs (ACDs), CDegs and complementary and alternative medicines (CAMs) were compiled from 5 hardcopy and 9 online resources, package inserts and published literature from Pubmed. The iphone web application was designed using Adobe software and open-source scripts, and served through a third-party server. ACD-CAM interactions (DCIs) searches were based on CReg acronyms. The application's interface fitted the iphone screen resolution of 320 × 480 pixels, and followed a longitudinal format to improve usability. The outcomes presented that OncoRx-Mi consists of a total of 256 CRegs which detects over 2500 CReg interactions with 166 CAMs classified into 8 categories. Majority of the DCIs are pharmacokinetic in nature (79%), involving the induction and inhibition of the cytochrome P450 isozymes (CYP2C9, 2C19, 2D6, 3A4) and p-glycoprotein. Pharmacodynamic HDIs include hepatotoxicity (39%), altered corticosteroid efficacies (30), as well as increased risks of hypoglycemia (4%), hypertensive crisis (2%), bleeding, and serotonin syndrome (1% each).

It is concluded that OncoRx-Mi is the first mobile web-based application of its kind which detects DCIs for combination CRegs. OncoRx-Mi will be continually updated to include interactions with various drug classes. It is hope that this database is useful for managing chemotherapy interactions in daily clinical practice, and can ultimately improve pharmaceutical care of cancer patients.



Fatigue

Evidence of a genetic association between a polymorphism in the I11 gene and sleep disturbance in oncology patients and their family caregivers (FCs)

The purpose of this study led by Dr. Christine Miaskowski was to identify whether genetic variations in IL-1 could impact levels of sleep disturbance in oncology patients and their FCs. In the study, DNA was recovered from plasma archived from 253 patients and FCs who participated in a descriptive longitudinal study of symptoms. The IL-1 (rs1143623) genotypes were

collected by TaqMAN Allelic Discrimination and the distribution of the polymorphism met Hardy-Weinberg expectations. Sleep disturbance was measured using the General Sleep Disturbance Scale. Differences in severity of symptoms between the 2 genotypes were evaluated using independent sample *t*-tests. The results showed that mean age of the sample was 61.4 years; 46% were male, and 75% were Caucasian. IL-1 genotype frequencies were 56.2% common allele homozygotes (GG), 3.6% rare allele homozygotes (CC), and 40.2% heterozygotes (GC). No sex differences were found in genotype distribution. Rare allele homozygotes for IL-1 reported significantly higher total sleep disturbance scores ($P = 0.01$), poorer sleep quality ($P = 0.003$), less sleep ($P = 0.02$), a higher number of early awakenings ($P = 0.02$), and higher levels of excessive daytime sleepiness ($P = 0.04$) at the initiation of radiation therapy than carriers of the common allele (i.e. GG + GC). The results provide preliminary evidence of a genetic association between a prominent cytokine and levels of sleep disturbance in a sample of oncology patients and their FCs. Carriers of the IL-1 monitor allele appear to have more sleep disturbance. Genotyping may identify high risk groups who warrant more targeted symptom management interventions.

Yocas yoga significantly improves multidimensional domains of cancer-related fatigue (CRF)

A nationwide, multi-site, phase II/III randomized controlled, clinical trial examining the efficiency of yoga for improving CRF among cancer survivors was performed by Dr. Karen Mustian, et al. In this study, cancer survivors with non-metastatic disease, suffering from moderate to high sleep disruption between 2-24 months post adjuvant therapy and who reported no participation in yoga during the prior 3 months were randomized into 2 arms: 1) standard care and 2) standard care plus the 4-week (wk) yoga intervention (2 x's/wk; 75 min./session). The yoga intervention utilized the University of Rochester (UR) Yoga Cancer Survivors (YOCAS®) program consisting of pranayama (breathing exercises), 18 gentle Hatha and Restorative yoga asanas (postures) and meditation. Cancer-related fatigue (CRF) was assessed pre- and post-intervention using the Multidimentional Fatigue Symptom Inventory.

The outcomes showed that 410 survivors were accrued (96% female, mean age = 54, 75% breast cancer). ANCOVAs with baseline values as covariates revealed significant differences between groups ($P < 0.05$) with yoga participants demonstrating greater improvements in total CRF (CS = +7.82, SE = 1.06) from pre- to post intervention compared to controls (total CRF CS = +2.34, SE = 0.91). Yoga participants also demonstrated significantly greater improvements in all sub-domains of CRF all ($P < 0.05$) including general fatigue (CS = -2.13, SE = 0.33), physical fatigue (CS = -2.02. SE = 0.27), emotional fatigue (CS = -1.72, SE = 0.31), mental fatigue (CS = -1.35, SE = 0.24) and vigor (CS = +0.60, SE = 0.28) from pre- to post-intervention compared to controls [general fatigue (CS = -0.47, SE = 0.28), physical fatigue (CS = -0.91, SE = 0.26), emotional fatigue (CS = -0.66, SE = 0.28), mental fatigue (CS = -0.47, SE = 0.22), and vigor (CS = -0.16, SE = 0.24)].

The conclusions come to that the standardized brief community-based YOCAS® intervention significantly improves physical, emotional and cognitive aspects of CRF. Clinicians should consider prescribing the standardized YOCAS program for survivors reporting CRF.

Evidence of possible biomarkers explain the mechanisms involved in fatigue

In Dr. Leorey Saligan's study, active protocol (NCT00852111) exploring fatigue symptoms in patients with localized prostate cancer and its relationship with changes in gene profiles before and after EBRT (external beam radiation therapy). Revised Piper Fatigue Scale was used to measure fatigue. Gene expression analyses using microarray using Affymetrix GeneChip® human genome U 133 Plus 2.0 array was conducted on the peripheral blood sample collected using Paxgene tube in 7 timepoints (baseline, first day after receiving first EBRT dose, day 7, day 14, day 21 or mid-EBRT, day 42 or end of EBRT, 1 month post treatment).

The results presented that fatigue scores of patients with localized prostate cancer peaked at day 21 (midpoint) of EBRT (mean = 2.78, SD = 2.02) and went down just above baseline (mean = 1.63, SD = 1.85) 1 month post treatment (mean = 1.70, SD = 2.88). Gene expression analyses using microarray of peripheral blood samples of individuals with prostate cancer reveal relationship between overexpression of genes that are related to inflammation, circadian rhythm, apoptosis and mitochondrial function and their fatigue symptoms as measured in several timepoints during localized radiation therapy. Dr. Leorey Saligan concluded that initial findings of an active fatigue study provide evidence of possible biomarkers that explain the mechanisms involve in fatigue. Future studies will explore possible interventional targets for novel therapies.

Infection

Hepatitis B screening and positivity prior to chemotherapy

Reactivation of hepatitis B virus (HBV) after chemotherapy occurs in patients positive for HBsAg or anti-HBc tests and can cause cancer treatment delays, liver failure, and death.

In this retrospective, cross-sectional study, by Dr. Jessica Hwang et al, M.D. Anderson databases were reviewed to identify new adult cancer patients between January 2004 and September 2007 who had received non-oral chemotherapy at least once in each of 2 consec-

utive months. The researchers determined the prevalence of screening for HBsAg or anti-HBc in the 2 months before or 1 month after initial chemotherapy. The differences in HBV screening and positivity between patients with solid tumors excluding hepatocellular cancer (solid non-HCC) and patients with hematological cancers were compared using chi square test.

The results showed that among 70,737 patients in the study period, 12,005 (17%) received chemotherapy. Of the latter, 53% were women, and there were 73% White, 12% Hispanic, 10% Black, and 3% Asian. Among those who received chemotherapy, 9862 (82%) had solid tumors and 2143 (18%) had hemotologic cancers. Overall, only 14% had HBV screening; 2% were HBsAg (+) and 9% were anti-HBc (+). HBV screening prevalence was significantly lower in solid non-HCC than hematologic cancer patients ($P < 0.01$). Prevalence of anti-HBc (+) was significantly higher among solid non-HCC than hemotologic cancer patients (13% *vs.* 6%, $P < 0.01$).

Therefore, HBV screening was conducted infrequently overall. Especially in patients with solid non-HCC. Anti-HBc positivity was significantly more common in patients with solid non-HCC cancers, despite the fact they were screened less frequently than patients with hemotologic cancers. Further studies are needed to identify factors that lead to low rates of HBV screening.

Continuous non-invasive monitoring of skin temperature during hematopoietic stem cell transplantation contributed in preventing neutropenic patients from sepsis by the timely detection of fever

Continuous skin temperature measurement by means of a Propaq® device appeared to be feasible and was validated compared to interval axillary measurements during allogeneic hematopoietic stem cell transplant. In June 2009, the continuous temperature measurements were implemented on the ward to monitor all allogeneic stem cell transplant recipients starting from the day of transplant until the onset of fever.

Continuous measurement was feasible for 29 (94%) of the 31 patients. However, 5 patients had already received empirical antibiotic therapy for fever that developed during the conditioning regimen, continuous measurements were > 0.5°C divergent from the simultaneously measured axillary temperature in 2 patients, and no measurements were done in 1 case because of technical problems. Of the 22 afebrile patients that started with the continuous measurements, 3 did not develop fever and 2 declined further measurements because of discomfort. Of the 17 patients that developed fever, the Propaq® alerted the nurse when the temperature rose in 11 cases. In the other 6 patients the Propaq® measurements was lower than the axillary measurement at the onset of fever, with differences up to 0.9°C.

In most cases the Propaq® temperature device contributed in preventing neutropenic patients from sepsis by the timely detection of fever. More research is needed to assess an adequate cut-off point to define non-invasively measured fever during neutropenia. It will be a challenge to develop an instrument for continuous measurement, more reliably correlated to core temperature.

Mucositis

A study validated the suitability of housekeeping genes for use in RT-PCR in an irinotecan-induced mucositis model

In this study led by Dr. Noor Al-Dasooqi, rats were treated with irinotecan and killed at different timepoints. H&E staining was performed to assess histopathological damage. RT-PCR was used to evaluate the expression of 11 housekeeping genes and results were analyzed using the Normfinder program to determine the expression stability of these genes. MMP-2 was used as a target gene to validate the appropriateness of the top ranking housekeeping genes.

Several of the genes under observation showed a very stable expression pattern. For normalisation to multiple housekeeping genes, the most stable combination across all time points following chemotherapy in the jejunum was Ywhaz/UBC and for the colon UBC/ACTB. SDHA and GAPDH were the most variable candidate genes in the jejunum and colon where they were 4.4- and 3.2-folds upregulated following irinotecan treatment, respectively.

This study validated the suitability of housekeeping genes for use in RT-PCR in an irinotecan-induced mucositis model. For normalisation in gene expression studies, a combination of Ywhaz/UBC and UBC/ACTB should be used in the jejunum and colon, respectively. UBC is the most favorable if restricted to a single housekeeping gene across all time points following irinotecan.

Clinical efficacy of visible-light therapy for the prevention of oral mucositis

The 2007 MASCC/ISOO systematic review[2] pointed that low-level laser therapy (LLLT) requires expensive equipment and specialized training; nevertheless, the panel was encouraged by the accumulating evidence in support of LLLT. Visible-light therapy (VLT) has a wide range of wavelength, including that of LLLT, while its cost is lower.

In Dr. Sharon Elad's study, a VLT-device that is adjustable for intra-oral use was applied in 20 patients undergoing HSCT. The study design was placebo-controlled, randomized, and double-blinded. Oral mucositis was assessed using OMAS and WHO scale. Oral pain and acceptance levels were scored by the patients using a 10-step ladder. Patients were evaluated once a week until day 21 post-HSCT. Mucositis rate, mucositis severity, and pain scores were compared between the 2 groups.

The results of the study showed that the mucositis rate

was lower in the treatment arm compared to the placebo arm (for both WHO and OMAS $P = 0.02$). Mucositis severity was milder in the treatment arm compared to placebo (for WHO $P = 0.04$; for OMAS $P = 0.01$). Patients in the treatment arm reported a significantly lower pain level compared to the placebo group ($P = 0.01$). The treatment was well tolerated with no adverse events related to the study device. Patients highly accepted this treatment modality.

In conclusions, these findings suggest that this VLT-device is safe and effective for the prevention of oral mucositis in patients undergoing HSCT.

Nutrition

Vitamin D insufficiency in cancer

Vitamin D insufficiency has been associated with cancer prognosis. Low levels may contribute to falls, fatigue, and muscle weakness. Risk factors include poor nutrition and northern latitude. Little is known about screening practices, prevalence and risk factors of vitamin D insufficiency in cancer. Dr. Katherine Hauser et al. investigated screening practices, prevalence and risk factors for vitamin D.

Electronic medical records of all adult solid tumor patients presenting in 2006-2007 were searched. The data extracted included: demographics, disease (primary, metastatic sites, comorbidity), and first 25 hydroxy vitamin D level (25OHD) during study period. Laboratory data, medications (anticonvulsants, antineoplastic, corticosteroids, vitamin D) and treatments (chemotherapy and radiotherapy) 2 months preceding the 25OHD were recorded. Clinical factors were compared between those tested for 25OHD *vs.* not, and those insufficient (25OHD $\leq$ 30 ng/mL) *vs.* not (25OHD > 31 ng/mL) by Chi square or T-tests. Stepwise logistic regression identified multivariable predictors of insufficiency.

The results of the investigation showed that 2097 of 39251 (5%) cancer patients had 25OHD done. They were more likely female (66% *vs.* 47%), and to have breast , hepatobiliary, skin or thyroid cancer (both $P < 0.001$). One thousand and four hundred-forty-three of 2097 (695) were insufficient. Insufficiency was associated with male gender, non Caucasian race, season, primary site, metastatic disease, low albumin, high bilirubin, high aspartate aminotransferase (AST), and no current antineoplastic or vitamin D medication (all $P < 0.05$). Comorbidities (osteoporosis, pathologic fracture) were associated with greater likelihood of supplementation and reduced risk of insufficiency. Multivariable predictors were non Caucasian race, season, primary site, low albumin, and absence of comorbidities, antineoplastic or vitamin D medication (all $P < 0.01$).

Therefore, vitamin D insufficiency was highly prevalent among cancer patients tested. Those at higher risk (male gender, non Caucasian race, upper GI/pancreatic cancers) were less often tested. Prescribed supplementation didn't completely protect against insufficiency.

Changing clinical practice to improve management of nutrition in women with gynaecologic cancer

Malnutrition is recognized as a significant dilemma in women diagnosed with gynaecologic cancer. A compromised nutritional state can increase risk of post surgical complications, resistance to infection and delayed wound healing. Limited research has been undertaken to develop standards of care to proactively address nutrition needs in women with gynaecological cancer. Dr. Mary Ryan et al. presented to results of a 3-phase study undertaken to improve clinical practice related to nutrition management in a gynaecology unit.

The study procedures were included as follows: phase 1: prospective assessment of nutritional status, physical conditioning and quality of life in women diagnosed gynaecologic cancer, using SF-36, PG-SGA, Symptom Distress Scale and International Physical Activity Questionnaire. Timepoints were at diagnosis, 3 and 6 months. Phase 2: retrospective medical record audit of nutritional assessment, documentation, and nutritional interventions in women with gynaecological cancer. A brief survey and focus group interview were conducted with clinical nurses about their knowledge, confidence, and current nutrition practice. Development of a clinical pathway and tailored education program for nurses reviewed by expert working group. Phase 3: evaluation of clinical pathway and education program.

The results showed that in phase 1, one-third of the women were indentified as having moderate or suspected malnutrition on PGS-A at diagnosis, with a small increase in this number over the time periods. Phase 2: nurses identified lack of confidence assessing this area of practice. Barriers to nutrition assessment identified were time, access to nutritional expertise, unclear guidelines of interventions to implement, when and who to refer. There was limited documentation of steps taken to address nutritional concerns. A clinical pathway and education program have been developed, and are being evaluated in phase 3 currently.

Nutritional assessment should be a standard component of care for women diagnosed with gynaecological cancer. Nurses are in a position to intervene early and reduce negative impact of cancer treatments on nutritional status, working with the multidisciplinary team.

Oncology Nursing

Supportive care needs and related factors in patients with advanced lung cancer

Dr. Yu-chien LIAO and her colleagues assessed the levels of supportive care needs in 5 domains, symptom severity and psychological distress, and determined the factors related to various need domains in advanced lung

cancer patients receiving active treatment.

In their study, 132 of advanced lung cancer patients were recruited using a cross-sectional survey from a medical center in Taiwan. Cancer Needs Questionnaire – Short from 32, Hospital Anxiety and Depression Scale (HADS) and Symptom Severity Scale (SSS) were used to assess supportive care needs, anxiety and depression as well as levels in 21 symptoms of the subjects. Logistic regression was applied to examine the related factors of unmet of supportive care needs in each domain.

The results showed that patients had mild to moderate levels of anxiety, depression and symptoms, but reported to have relatively high level of unmet care needs with an average score of 42.5 (SD 18.9) in a 100-point scale. A large proportion of patients (89%) reported with unmet needs in information and health care system, followed by psychological care (69.9%) and patient care and supports (59.4). Likewise, 46.6% of patients had needs in physical and daily living care and about 1/5 of subjects had unmet needs in communication. Among those factors related to the patients' unmet care needs, symptom severity, anxiety, depression, performance status and younger age were identified as the significant factors related to unmet supportive care needs. Therefore, advanced lung cancer patients perceived high levels of supportive care needs which were mainly related to symptom severity and psychological distress. A systematic assessment of these problems and strategies to meet supportive care needs are recommended to further development of an evidence-based lung cancer care model.

Development and validation of the health beliefs and medication adherence in breast cancer scales

Non-adherence to aromatase inhibitors (AIs) decreases treatment effectiveness in up to half of breast cancer survivors (BCS) and is amenable to nursing intervention. Health beliefs (HBs) are important in understanding adherence. The purpose of Dr. Carrire Striker's study was to adapt and validate the Champion Health Belief Model Scales (CHBMS) for use in understanding adherence to AIs.

The Health Belief Model (HBM） guides this study. Items were generated based on literature review and HBM for 4 subscales consistent with the CHBMS: 1) perceived susceptibility (PSus) and 2) perceived severity (PSev) to/of cancer recurrence, and 3) perceived benefits (PBen) of, and 4) perceived barriers (PBar) to AI therapy. Items were reviewed for content validity by breast oncology and behavioral medicine experts. Resulting subscales were administered to 20 postmenopausal BCS receiving AIs to assess face validity, and cognitive interviews (CIs) evaluated item clarity, acceptability, and completeness. Internal consistency was assessed among a sample of 100 BCS, and item reduction proceeded according to criteria from Nunnally (1978). Finally, principal axis factor analysis with quartimin rotation was performed with data from 490 BCS receiving AIs.

The results showed that minor revisions were made based on expert review and CIs, and the PSev scale was discarded due to poor item variability and consistent with revised HBM. In 100 BCS, the 3 subscales (PSus, PBen, PBar) had internal consistency reliabilities of $\alpha = 0.86$, 0.81, and 0.85. Principal axis factor analysis confirmed the 3 factors with eigen values greater than 1.0 accounting 45.3% of the variance in health belief scores once 1 item was removed. Final scales are PSus (9 Items, 0.81), PBar (3 Items, 0.79) and PBen (3 Items, 0.82).

Therefore, the HBMABC subscales assess health beliefs related to medication adherence in postmenopausal BCS and demonstrate adequate content/face validity, acceptability, internal consistency, and replicated in factor analysis, and may be useful in understanding HBs and adherence to AIs, a nursing sensitive patient outcome.

Oral Care

Stimulated salivary flow deceases in patients undergoing HSCT (hematopoietic stem cell transplantation)

A study led by Dr. Adrian Ramseier aimed to record and analyze stimulated salivary flow rates before and 6, 12 and 24 months after HSCT. Based on clinical experience it was hypothesized that hyposalivation is a common problem among HSCT recipients.

In the study, stimulated salivary flow rates of HSCT recipients (209 male, 143 female, median age 45.6 years, range 16-77 years) were examined pre-HSCT and 6, 12 and 24 months post-HSCT ($n = 352$, 144, 134 and 96 respectively). Seventy generally healthy registered stem cell donors (37 male, 33 female, median age 45.9 years range 22-61 years) served as controls. Subjects chewed a neutral paraffin gum continuously for 6 min. After 1 min, whole salivary flow was measured for 5 min, converted to mL/min, and analyzed statistically using Wilcoxon Rank Sum Test.

The results of the study demonstrated that hyposalivation (≤ 0.7 mL/min) was found in 35%, 55%, 30% and 25% of the recipients at pre-HSCT and 6, 12 and 24 months post-HSCT, respectively. In comparison to the control group with 16% the differences were statistically significant at pre-HSCT and 6, 12 and 24 months post-HSCT ($P < 0.00001$). Severe hyposalivation with a flow rate of ≤ 0.3 mL/min was found in 18%, 4% and 5% of the recipients 6, 12 and 24 months after HSCT, respectively.

It is concluded that hyposalivation seems to be a common but usually reversible problem among HSCT-recipients. However, some patients suffer from persisting severe hyposalivation.

Medical ozone (O3) oil or gas applications heal osteonecrosis of the jaw (Onj) in patients treated with bisphosphonates (Bps)

Dr. Carla Ida Ripamonti and her colleagues evaluated the efficacy and safety of medical ozone therapy in treating ONJ in patients with bone metastases treated with Bps in the absence of odontoiatric preventive measures. In the study, patients with breast cancer (16), prostate (5), lung cancers (2), NHL (1), multiple myeloma (2) with ONJ were treated with O3 oil or gas application. All the patients were in a stable disease without progression; 10 of them had ONJ lesions ≤ 2.5 cm. O3 oil suspensions application on ONJ lesions ≤ 2.5 cm was carried out with localized applications directly on the lesions; patients with larger lesions (≥ 2.5 cm) were treated with ozone gas locally applied. All the patients received treatments every third day and all of them were previously treated with antibiotic therapy (azithromycin, 500 mg/day) for 10 days. The statistical analysis is based on a Simon two-stage design, the second stage is on-going. In this preliminary analysis , Dr. Ripamonti focus on 10 patients treated with O3 oil with a medium follow up of 8 months, and 16 patients on medical gas ozone.

In the results of the study, 79% of the patients (n = 19) showed complete response in terms of radiological lesion disappearance with complete reconstruction of oral tissue. Among them, 16 patients developed spontaneous sequestrum with expulsion of the necrotic bone whereas in 3 patients with large extension of bone involvement, surgical intervention was necessary. Seventy percent of the patients treated with O3 oil experienced a complete response of 4 applications whereas patients treated with gas needed 4 to 19 applications. No patients presented adverse events related to the use of ozone treatments. Six patients are still on treatment and are improving as well.

Therefore, few application of O3 oil suspension in patients with smaller lesions and gas medical ozone for wider lesions can rapidly lead to complete healing of ONJ.

Pain Management

A systematic analysis of the in vitro effects of opioids on natural killer cell function

A range of opioid analgesics are commonly used in the treatment of cancer pain. In addition to modulating the transmission and perception of pain, opioids can also affect other organ-systems and cause toxicity. Although in-vitro and in-vivo studies have shown that certain opioids can influence the immune system, and there have been no comparative, systematic studies analyzing their impact. The effect on opioids on immune function is an important issue, as opioid choice might influence the outcome of the patients with disease, such as cancer. Natural killer (NK) cells are vital in the immunosurveillance and control of cancer and murine studies have shown tramadol to enhance NK cell cytotoxicity and reduce tumor load. In contrast, morphine appears to inhibit NK cell activity. It remains unclear whether the immunoregulatory properties of opioids are mediated via central mechanisms or via direct effects on immune cells.

A study led by Dr. Jason Boland evaluated the direct (in-vitro) effects of morphine, tramadol, fentanyl, buprenorphine and oxycodone on NK cell cytotoxicity using concentrations of each opioid which approximated to those that are present clinically. Mononuclear cells (PBMCs) were isolated from the peripheral blood of 3 healthy volunteers and activated for 3 days with IL-2. The capacity of IL-2 activated PBMCs to kill fluorescently labeled K562 cells (a erythroleukaemic cell line) which are sensitive to NK cells was then determined using a flow cytometry assay.

None of the opioids tested had any effect on NK cell cytotoxicity. Therefore, these findings suggest that any effects which opioids might have on NK cell cytotoxicity are most likely mediated via indirect mechanisms, possibly by a central action causing the release of immunosuppressive mediators. The effects of opioids on NK cell function need to be systematically studied in patients with cancer before any definitive conclusions can be drawn about the clinical relevance of opioid-induced NK cell modulation.

Psychological and clinical predictive factors for post-mastectomy pain syndrome (PMPS)

Dr. Florence Dixmerias's study aimed to better define clinical and psychological factors predictive of PMPS. A prospective, multicentre study was performed with 154 patients requiring breast cancer surgery (tumorectomy or mastectomy with lymph nodes dissection). Clinical assessments including pain evaluation and description, and psychological evaluations using the following psychological variables: neuroticism, suppression of negative feeling, alexithymia, dramatization, avoidance, perceived concern, emotional distress, were performed at different time periods (one day before surgery, H2, D1, D6, 6 months). At 6 months, PMPS was diagnosed according to Watson's criteria[3]. A logistic regression was conducted to analyze predictive factors.

The results showed that 65% of patients were symptomatic at 6 months (dysesthesia or pain). A PMPS was found in 49% of patients. Significant PMPS risk factors were: presence of preoperative pain (P = 0.006), post-operative morphine titration (P = 0.001), distant memory of post-operative pain (P = 0.001), greater preoperative dispositional anxiety (P = 0.01), low control of preoperative sadness (P = 0.001), high level of post-operative dramatization (P = 0.01), and post-operative anxio-depressive disorders (P = 0.001).

Therefore, the interaction of some clinical and psychological factors may explain the development of

chronic pain after breast cancer surgery. Identification of these factors and a more global interdisciplinary care from diagnosis for these at risk patients could prevent pain from becoming chronic.

Palliative Medicine

Availability and integration of palliative care in United States Cancer Centers

The current state of palliative care (PC) in cancer centers in the United States is not known. A survey was used by Dr. David Hui to determine the availability and degree of integration of PC services and to compare between National Cancer Institute (NCI) and non-NCI cancer centers.

Both cancer center executives and PC clinical program leaders (where PC available) of all 71 NCI designated cancer centers and a random sample of 71/1411 non-NCI centers regarding their PC services were investigated. Executives were also asked about their attitudes toward PC.

The results showed that the response rate was 71% (101/142) for executives, and 81% (96/118) for PC program leaders. Eighty-nine of 101 (88%) executives reported an active PC program. NCI cancer centers were significantly more likely to have a PC program (98% *vs.* 78%, $P = 0.002$), at least one PC physician (90% *vs.* 56%, $P < 0.001$), an inpatient PC consultation team (92% *vs.* 56%, $P < 0.001$), and an outpatient PC clinic (59% *vs.* 22%, $P < 0.001$).

Few cancer centers had dedicated PC beds (23%) or an institution-operated hospice (36%). The median reported time from referral to death was 7 (Q1-Q3 4-16) days for consult teams, 7 (Q1-Q3 5-10) days for inpatient units, and 90 (Qi-Q3 30-120) days for outpatient clinics. Among NCI centers with PC, fewer than half had research programs (46%), PC fellowships (38%), or mandatory PC rotations for oncology fellows (28%). Poor reimbursement (63/101, 62%) and limited institutional resources (62/101, 61%) were the most commonly cited barriers to PC access. The median support (0 = strongly disagree, 10 = strongly agree) among executives was 10 (Q1-Q3 8-10) for stronger integration, and 8 (Q1-Q3 7-10) for PC research funding.

In conclusion, most cancer centers reported a PC program, although only a small percentage had designed inpatient beds, outpatient services, fellowship positions or rotations for oncology fellows. Further effort is necessary to consolidate PC in oncology practice.

Symptom burden, palliative care referral and quality of care for phase I cancer patients

Phase I (P1) trials offer advanced cancer patients the opportunity to pursue further life-prolonging cancer treatments. In Dr. David Hui's retrospective cohort study, symptom burden, timing of referral and quality of end-of –life care between patients referred to palliative care (PC) by P1 oncologists and those referred by non-phase I oncologists (NP1) were compared.

All 57 patients with advanced solid tumors referred by P1 to the PC outpatient clinic in M. D. Anderson Cancer Center in 2007/2008 were concluded. The comparison cohort consisted of 114 NP1 patients stratified by age, sex and cancer diagnosis in a 1:2 ratio. The information regarding patient characteristics, Edmonton Symptom Assessment Scale (ESAS), timing of referral, admissions and cancer treatments were retrieved.

Both cohorts had the following matched characteristics: average age of 57 years, female 44%, and gastrointestinal cancers 47%. At the time of PC consultation, P1 patients had better performance status (ECOG 0-1, 61% *vs.* 36%, $P = 0.003$) than NP1 patients. ESAS did not differ between P1 and NP1, except for better well being in P1 patients (mean 4.5 *vs.* 5.5, $P = 0.03$). No difference was detected for the duration between hospital registration and PC consult (409 d *vs.* 340 d, $P = 0.41$) and overall survival from time of PC consult (137 d *vs.*116 d, $P = 0.45$). Among all the patients who died, those referred by P1 were more likely than the NP1 cohort to receive chemotherapy within the last 30 days of life (31% *vs.* 13%, $P = 0.014$). Differences in the incidence of intensive care unit admissions (4% *vs.* 6%, $P > 0.99$) or in-hospital deaths (18% *vs.* 28%, $P = 0.21$) between the 2 groups were not detected.

Therefore, P1 outpatients referred to PC had a better performance status and were more likely to receive chemotherapy at the end-of-life compared to NP1 patients. P1 involvement did not delay PC referral. This supports the development of a simultaneous care model.

Psychosocial

Religion and spirituality in cancer patients cared for in oncological, supportive care, psychological and rehabilitation units

A study led by Dr. Carla Ida Ripamonti evaluated the importance of religion/spirituality among cancer patients in supportive care or rehabilitation settings. The SBI-15R was used, which was a brief self-report inventory designed to measure religious and spiritual beliefs and practices and the social support derived from a community sharing those beliefs.

Two hundred and fifty-seven patients cared for in the Oncological, Supportive Care, Psycho-Oncology and Rehabilitation settings were involved in this study.

The results of the study showed that the sample has a mean age of 53.6 years, 74% were female, and 49% were churchgoers mainly Catholics. Regarding beliefs and practices: a) 91% strongly/somewhat agree that, "God in some form exists"; b) 80% strongly/somewhat agree that, "Religion is important in my day-to-day life" c) 79% strongly/somewhat agree to have experienced

peace of mind through their prayers and meditation; d) 76% strongly/somewhat agree that, "During times of illness, my religious or spiritual beliefs have been strengthened".

As far as social support from the religious community is concerned: a) 68% strongly/somewhat agree, "I enjoy attending religious functions held by my religious or spiritual group"; b) 57% strongly/somewhat agree, "When I feel lonely I rely on people who share my spiritual or religious beliefs for support"; c) 47% all of the time/ a good bit of the time, "Enjoy meeting or talking with people who share my religious or spiritual beliefs" ; d) 16% all of the time/a good bit of the time seek out people in their religious or spiritual community when they need help.

The results of the study showed how important religion is for cancer patients, even in non-advanced stages. However, these patients live often their spiritual life by one's self, because they do not find comfort in speaking with people sharing the same beliefs or even they do not ask their religious and spiritual community for help.

Psychosocial aspects of cancer survivorship

Dr. Tammy Weitzman et al. summarized the literature regarding psychosocial survivorship as part of their contribution to the forthcoming MASCC publication, *A Handbook of Cancer Supportive Care and Survivorship.* A systematic search of the literature was conducted to identify sources that described psychosocial survivorship, specifically the psychological, emotional, and social consequences of cancer and its treatment.

They found that the majority of research on psychosocial survivorship has focused on rates of Adjustment Disorder, Depression, Anxiety, and Posttraumatic Stress in cancer survivors. Adjustment Disorder is a maladaptive reaction to an identifiable psychosocial stressor that can occur within 3 months after onset of that stressor. It is common and affects as many as 22.6% of the cancer survivorship population. Rates of Depression (10%-25%), Anxiety (0.9%-77%), and Posttraumatic Stress (0%-32%), in contrast, vary widely across study findings. This is likely due to the many methodological limitations present in this type of research (e.g., small sample sizes, varying assessment instruments and modalities). Research with pediatric cancer survivors utilizing a much more standardized approach toward assessment of psychosocial sequelae has found that a significant proportion of pediatric survivors experiences difficulty with psychological distress and health-related quality of life.

In the conclusion, Dr. Weitzman demonstrated that cancer survivors clearly experience both short- and long-term psychological effects stemming from their cancer experience. The efforts as oncology clinicians should be focused on improving knowledge base about the various psychological, emotional, and social consequences of cancer and its treatment. Early identification of these issues in patients receiving cancer care is critically important if we consider that psychological/emotional/social complications can negatively impact patients' quality of life over time. Moreover, efforts as oncology researchers should be focused on conducting prospective, longitudinal research with standardized assessment instruments to confirm previous findings and inform future efforts at intervention throughout critical points in survivorship.
Please look for the details of some of the presentations presented at the 2010 MASCC Symposium in the coming issues of the journal of Supportive Care in Cancer.

Conflict of interest statement

No potential conflicts of interest were disclosed.

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