Side effects and quality of life
REDUCING SYMPTOM BURDEN, PAIN AND COGNITIVE DECLINE

Katarzyna J. Jerzak, MD, FRCPC, Medical Oncology Fellow, University of Toronto; and Kathleen I. Pritchard, MD, FRCPC, Medical Oncologist, Sunnybrook Odette Cancer Centre

**TRIAL SUMMARY: Symptom burden**


In this study, one of the largest quality of life (QOL) analyses conducted in the current framework of breast cancer treatment, researchers at Sunnybrook Health Sciences Centre sought to determine QOL and symptom burden (SB) among breast cancer patients related to disease stage, type of treatment and disease-free interval. Patients completed the Edmonton Symptom Assessment System (ESAS) and the Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B) and were categorized into 4 groups based on their stage of cancer: ductal carcinoma in situ (DCIS), early stage, locally advanced or metastatic. Patients within these groups were divided into subsequent cohorts based on their last day of treatment (<2 years, 2 to <5 years, 5 to <10, ≥10 years), age at time of enrolment (≤50, 51 to 60, 61 to 70, and ≥70 years), surgery type (lumpectomy or mastectomy), radiation type (5000 cGy/25, 4256 cGy/16 or 4250 cGy/16 and 9000 cGy/1), chemotherapy and hormone therapy. Patients were also stratified by recurrence status and time since diagnosis of primary cancer.

**Results:** Between January to August 2014, a total of 1,513 patients were enrolled. Metastatic patients (n=178) had the highest ESAS scores compared to all other patient groups and higher scores of depression and anxiety compared to DCIS (n=141) and early-stage patients (n=769). Patients in the 2 to 5 years (n=255) or 5 to 10 years post-treatment cohort (n=214) had lower QOL scores than those in the ≥10 years cohort (n=101). Patients aged 50 and under with early-stage cancer (n=171) or locally advanced cancer (n=145) had higher ESAS scores for tiredness, depression and anxiety compared to all other age cohorts, as well as overall lower QOL. Patients treated with a lumpectomy (n=790) had significantly higher QOL scores (except for social/functional wellbeing) than those treated with mastectomy (n=611). Early-stage patients who received chemotherapy (n=373) reported more ESAS symptoms and an overall lower QOL compared to those with no chemotherapy (n=389). Patients taking selective estrogen receptor modulator (SERM) treatments (n=438) had higher depression and lower QOL compared to those not on SERMs (n=528). Patients with aromatase inhibitor treatment (AI; n=512) had lower depression and higher QOL compared to those not on AIs (n=454).

Patients under 50 years old treated with mastectomy, chemotherapy or SERM hormone therapy had increased SB and decreased QOL in the 2 to 10 years post treatment. The authors suggest that individualized interventions and programs be developed to tailor to physical, educational and psychosocial needs identified across the breast cancer continuum.
**TRIAL SUMMARY: Acute pain syndrome**


Taxane acute pain syndrome (TAPS) is characterized by myalgias and arthralgias starting 2 to 4 days after taxane chemotherapy and lasting 5 to 7 days. Despite significantly impacting quality of life (QOL) and occurring in approximately 55% and 33% of patients receiving paclitaxel and docetaxel, respectively, little is known about its optimal management. This systematic review of trials reporting the treatment of TAPS in patients undergoing chemotherapy for breast and prostate cancers looked at outcome measures including treatment type and response of myalgias, arthralgias, pain and QOL measures.

**Results:** Of 1608 unique citations initially identified, 4 studies were included in the final analysis. Randomized placebo-controlled trials (273 patients) and retrospective studies (10 patients) were included. Agents investigated were: gabapentin (300 mg orally tid), amifostine (910 mg/m² intravenously), glutathione (1.5 g/m² intravenously) and glutamine (10 grams orally t.i.d.). Sample sizes ranged from 10 to 195. Pain response rates for each agent were: gabapentin (90%), amifostine (36%; 95% CI, 16% to 61%). Response to glutathione and glutamine were no different from placebo. Two trials reporting QOL outcomes showed no statistical differences between the two arms studied with regards to symptom distress-scale scores and pain questionnaire items. The authors conclude that TAPS remains poorly researched, with few studies evaluating its optimal management. More studies and standardized tools are required to prospectively compare treatment strategies and potentially identify risk factors for TAPS.

**TRIAL SUMMARY: Timing the onset of cognitive impairment**


While chemotherapy-related cognitive impairment (CRCI) is increasingly recognized, questions remain regarding the timing of onset. The objective of this study was to utilize surrogate cognitive markers to assess CRCI immediately following chemotherapy administration. Patients aged 18 to 80 years receiving intravenous (IV) chemotherapy for any stage of breast or colorectal cancer were eligible for the study. Patients with brain metastasis, neurologic disorder or allergic reaction to chemotherapy were excluded. Patient symptoms, peripheral neuropathy and Stanford Sleepiness Scale were assessed. Cognitive testing with a 5-minute psychomotor vigilance task (PVT) and trail-making test B (TMT) was completed on a tablet computer pre-chemo-therapy and immediately post-chemotherapy. Paired Wilcoxon Rank Sum tests were used to assess change in median PVT reaction time, TMT completion time, TMT errors and PVT lapses. Patients with median PVT reaction times slowed by over 20 ms (similar to the change in reaction time after ingestion of alcohol) were identified. Spearman’s rank correlation was used to assess factors associated with PVT changes.

**Results:** The study included 50 patients with a median age of 52. Post-chemotherapy median PVT reaction time slowed by an average of 13.8 ms (p=0.075) and by over 20 ms in 27 patients (36%). TMT completion post chemotherapy was faster by an average of 3.1 seconds (p=0.004). No differences were seen in TMT errors (p=0.857) or PVT lapses (p=0.874). Change in median PVT reaction time was not associated with age, number of prior chemotherapy cycles, peripheral neuropathy grade, or self-reported anxiety, fatigue or depression. No significant overall impairment in median PVT reaction time was demonstrated, but impairment correlating to effects of alcohol was seen in 36% of patients. This effect appears independent of age, self-reported symptoms or prior chemotherapy cycles. Further studies assessing functional impact of immediate-term CRCI are warranted.

**COMMENTARY:** Historically, the QOL of cancer patients has been challenging to study due to a lack of standardized tools and measures. In a clinical trial setting, high costs and limited resources are also restrictive. It was a Canadian trial, TAX 327, led by Dr. I. Tannock, that overcome these challenges, showing that docetaxel plus prednisone prolonged survival and improved the QOL compared to mitoxantrone plus prednisone in men with castrate-refractory prostate cancer.¹ This study not only changed the global standard of care for advanced prostate cancer, but also ignited an interest in supportive care research in Canada.

The 2015 CAMO Annual Scientific Meeting highlighted three abstracts focused on symptom control and QOL. Dr. Sunil Verma and his team reported on the QOL and symptom burden (SB) of over 1,500 patients with breast cancer.² They found that women <50 years of age and those with metastatic disease had higher scores for depression and anxiety than their older counterparts with early breast cancer or ductal carcinoma in situ (DCIS). Further, a group of patients who were treatment-free for 2 to 10 years had a lower QOL than those who were treatment-free for more than 10 years. This study highlights the importance of comprehensive patient assessment that includes psychosocial evaluation and the need to monitor long-term implications of breast cancer therapies.

Dr. Fernandes and his team evaluated treatment options for taxane-induced pain, which occurs in up to 58% of patients³ and may result in dose reductions or even discontinuation of chemotherapy. Their systematic review yielded 4 studies with only 283 patients among them.⁴ The most effective drug was gabapentin, which reduced pain in 90% of patients; however, only 10 patients were evaluated and
efficacy was determined retrospectively. Other neuropathic pain agents, such as duloxetine (which is an effective therapy for platinum-induced pain), have not been studied, and neither have commonly-prescribed narcotics. Prospective studies to identify the optimal treatment of taxane-induced pain would be of great value to our patients.

Dr. Khan and his team studied the immediate cognitive impact of IV chemotherapy in 50 patients with either breast or colorectal cancer. Participants were treated in the adjuvant and metastatic settings, but their chemotherapy regimens were not explicitly specified. Study investigators found that 36% of patients demonstrated a longer reaction time (as measured by a psychomotor vigilance test) immediately after chemotherapy compared to their baseline assessment. The observed delay in reaction time was comparable to having a blood alcohol level between 0.5 g/L and 0.8 g/L (the legal limit for driving in Ontario is 0.8 g/L). Further characterization of this acute form of “chemo brain” and its potential safety implications is required.

Although studying QOL in oncology is challenging, research in this area must be intensified due to a high potential for significant, and often immediate, clinical implications. According to Steve Jobs, former CEO of Apple who succumbed to pancreatic cancer, “Quality is more important than quantity. One home run is much better than two doubles.”

References