### Chemotherapy-specific health status measures

<table>
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<th>Questionnaire</th>
<th>Acronym</th>
<th>Description</th>
<th>Free to non-commercial research?</th>
<th>Validation with cancer patients</th>
<th>Examples of cancer studies where instrument identified an effect</th>
</tr>
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</table>
| Breast Cancer Chemotherapy Questionnaire | BCQ | 30 items, covering:  
• Consequences of hair loss  
• Emotional dysfunction  
• Physical symptoms  
• Trouble/inconvenience  
• Fatigue  
• Nausea  
• Positive well-being | ? | In 418 women with Stage II breast cancer:\(^1, 2\)  
**Validity**  
Concurrent – correlations with SF-36 physical (0.58) and emotional (0.60), Spitzer (0.62), Karnofsky (0.46).  
Known groups - identified a difference between women whose treatment had ended and those still on treatment (p < .0001, n=112) suggestive of responsiveness; no such difference was identified by the SF-36 or Spitzer.  
**Reliability**  
Mean change score in stable patients = -0.183 (n=184)  
In 164 women with lymph-node positive breast cancer:\(^3\)  
**Validity**  
Predicted early treatment discontinuation even after accounting for age and chemotherapy-related side effects | \(^4, 5\) |
| FACT and Gynecology Oncologic Group Neurotoxicity Questionnaire | FACT&GOG -Ntx | The FACT-G (27 items) plus an 11-item subscale that evaluates symptoms and concerns associated with chemotherapy-induced neuropathy (sensory, hearing, motor and and) | Yes | In 99 women with (mostly Stage III) ovarian cancer, 43 of whom had known chemotherapy-induced neuropathy, the Ntx subscale demonstrated:\(^6\)  
**Validity**  
Known groups – distinguished between chemotherapy naive and known neuropathy groups.  
Concurrent –showed mostly moderately significant correlations with objective measures of neuropathy.  
Responsiveness - showed a non-significant correlation with overall ratings of worsened, stable and improved.  
**Reliability** | \(^12\) |
dysfunction) Internal consistency – Cronbach’s alpha >0.70 in 11/12 assessments.

In 134 women with recurrent gynaecologic cancer on doxorubicin/cisplatin/Paclitaxel (TAP) therapy, the Ntx subscale demonstrated:

Validity
Construct validity – correlations between each item and overall subscale increased towards end of treatment (r= 0.60 – 0.80).

Criterion - area under the receiver operating characteristic curve was 0.81 for the Ntx score prior to cycle 3.

Known groups – identified a significant difference (p< 0.001) between the TAP group and women treated with doxorubicin/cisplatin after 2 cycles.

Responsiveness - Significant (p <0.001) change in scores from baseline to prior to cycle 7.

Reliability
Internal consistency – Cronbach’s alpha 0.80 – 0.85 across 7 data points from baseline to prior to cycle 7.

NB – similar validity, responsiveness and reliability was reported for a 4 item shortened version of the FACT/GOG-Ntx that includes only sensory items.

In women with advanced epithelial cancer, Ntx subscale demonstrated:

Validity
Predicted tolerance to intraperitoneal (IP) chemotherapy

In 202 patients with relapsed, refractory multiple myeloma:

Validity
Predicted survival.

In patients with relapsed and/or refractory myeloma treated with bortezomib, Ntx subscale demonstrated:

Responsiveness - Identified changes through treatment emergent neuropathy and resolution to baseline following discontinuation.
In 230 patients with advanced nonsmall cell lung carcinoma on taxane therapy, Ntx subscale demonstrated:11

Responsiveness (n=143) - Identified significant (p=0.000) decline over 12 weeks of treatment.

Reliability
Internal consistency – Cronbach’s alpha 0.82– 0.86

| FACT Taxane Questionnaire | FACT-Taxane | FACT&GOG-Ntx plus 4 items specific to the effects of taxane therapy including swelling of limbs, pain in fingertips and concern about appearance of hands. | Yes | In 230 patients with advanced nonsmall cell lung carcinoma on taxane therapy, Ntx subscale demonstrated:11

Responsiveness (n=143) - Identified significant (p=0.000) decline over 12 weeks of treatment.

Reliability
Internal consistency – Cronbach’s alpha 0.84 – 0.88 |

| GLQ-8 | GLQ-8 | 8 items covering: anxiety/depression, nausea, numbness/pins and needles, hair loss, tiredness, appetite/sense of taste, sexual interest or ability, thought of having treatment, with an option to include any additional issue of the patient’s | Yes | In 166 patients with mixed cancer diagnoses starting/on chemotherapy: 14

Validity
Content – only 5% of patients identified a problem not included in the GLQ-8 as the most important.

Factorial validity - analysis yielded a 6 factor solution.

Known groups – patients on chemotherapy performed worse on all items except anxiety/depression than those not on chemotherapy.

Responsiveness – Changes in anxiety/depression, nausea and thought of treatment were significantly correlated with changes in UICC/ECOG performance status.

Reliability
Test-retest – at 1 hr, 0.68-0.96; at 24 hrs, 0.69-0.92. |
choosing. Patients are asked to rate which problem is most important.

In 103 patients with mixed cancer diagnoses and undergoing a range of treatments:\[^15\]

**Validity**
Convergent – all items except hair loss correlated significantly with scores on the Functional Living Index of Cancer (FLIC), Perceived Adjustment to Chronic Illness Scale (PACIS) and the Psychological Adjustment to Cancer (PAC). The anxiety/depression item correlated highly with the Hospital Anxiety and Depression Scale (HADS) and Profile of Mood States (POMS).

Known groups – younger patients scored significantly more poorly on the anxiety/depression, appetite and thought of treatment items.

In 152 patients with metastatic melanoma undergoing chemotherapy plus/minus interferon:\[^16\]

**Validity**
Predicted survival

In 125 patients with metastatic melanoma undergoing a range of treatments:\[^17\]

**Validity**
Predicted survival.

<table>
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<tr>
<th>Subjective Chemotherapy Impact Scale</th>
<th>SCI</th>
<th>Asks patients to indicate how many days in each cycle they had ‘discomfort’ and how many days they ‘almost wished to eliminate’</th>
<th>Yes</th>
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<tbody>
<tr>
<td>In 168 Italian women with breast cancer undergoing chemotherapy:[^19]</td>
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**Validity**
Responsiveness – scores were significantly different (p <0.002) at day 1 and day 8 of treatment.

Known groups – distinguished between patients grouped according to different drug regimes.

Concurrent (n=24) – number of days of discomfort was significantly correlated (p<0.05) with number of hours of nausea.

**Reliability**
Test re-test – r = 0.39 |
Worthing Chemotherapy Questionnaire

**WCQ-75**

75 items covering six domains: digestive system, mouth and nose, skin and hair, eyes, general physical health, moods and feelings

? In 90 patients undergoing chemotherapy regimes known to cause stomatitis:

**Validity**

Factorial validity - K-M-O value for the matrix was 0.85. The Bartlett value was 575 (P < 0.00001).

Responsiveness (n=30) – scores on ‘mouth problems’ significantly decreased following termination of treatment.

Reliability (n=27)
Test re-test – for 30 randomly selected items repeated after 24 hrs, k=0.67 to 0.98

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**References**

1. Levine M, Guyatt G, Gent M, et al. Quality of life in stage II breast cancer: an instrument for clinical trials. *J Clin Oncol.* 1988;6(12):1798-1810 A questionnaire has been developed for use as an outcome measure in clinical trials of adjuvant chemotherapy in women with stage II breast cancer. The selection of items for this Breast Cancer Chemotherapy Questionnaire (BCQ) was based on the problems and experiences felt to be most important by women undergoing adjuvant chemotherapy. The BCQ consists of 30 questions that focus on loss of attractiveness, fatigue, physical symptoms, inconvenience, emotional distress, and feelings of hope and support from others. The BCQ, other instruments that evaluate quality-of-life (Spitzer, Karnofsky, and Rand), and patient and physician global assessments were administered serially to 418 patients taking part in a randomized trial comparing a 12-week regimen and a 36-week regimen of adjuvant chemotherapy. The validity of the BCQ is supported by its correlation with the Rand Emotional (r = .58), Rand Physical (r = .60), and Spitzer (r = .62) questionnaires. The BCQ correlated more strongly with global ratings of both physical and emotional function by the patients and their physicians than the other instruments. A comparison of the quality-of-life outcomes of patients in the two treatment groups in the period beyond 3 months after initiation of treatment, when one group had completed the treatment course and the other was still on treatment, revealed that the BCQ and Karnofsky were the only instruments able to demonstrate differences between the groups (P less than .0001). Hence, the BCQ is a valid and responsive method of assessing treatment-related morbidity in patients receiving adjuvant chemotherapy for stage II breast cancer.

2. Guyatt GH, Deyo RA, Charlson M, Levine MN, Mitchell A. Responsiveness and validity in health status measurement: a clarification. *Journal of Clinical Epidemiology.* 1989;42(5):403-408 We present data from two studies which clarify the relationship between the responsiveness and validity of instruments designed to measure health status in clinical trials. In a controlled trial of long vs short duration adjuvant chemotherapy for women with Stage II breast cancer, the Breast Cancer Chemotherapy Questionnaire (BCQ) proved valid as a measure of subjective health status and was able to distinguish long vs short arms. Well validated measures of physical and emotional function developed by the Rand Corporation were unable to distinguish between the two groups. The Eastern Co-operative Oncology Group Criteria (ECOG) distinguished the two groups, but failed criteria of clinical sensibility as a measure of subjective health status. In a study of patients with Crohn’s disease and ulcerative colitis, the Inflammatory Bowel Disease Questionnaire (IBDQ) showed small intrasubject variability over time. Global ratings of change showed moderate to high correlations with changes in IBDQ score, and patients who reported overall improvement or deterioration showed large changes in IBDQ score. Each of these findings support, in different ways, the reproducibility, validity, and responsiveness of the questionnaire. While the same data can at times bear on both validity and responsiveness, when assessing evaluative instruments it is useful to make a conceptual distinction between the two.
Richardson LC, Wang W, Hartzema AG, Wagner S. The Role of Health-Related Quality of Life in Early Discontinuation of Chemotherapy for Breast Cancer. *Breast Journal.* 2007;13(6):581-587. To examine the role of health-related quality of life (HRQOL) in early treatment discontinuation among women enrolled in a breast cancer clinical trial. A total of 464 women were enrolled in the Eastern Cooperative Oncology Group randomized controlled trial of adjuvant regimens comparing six cycles of cytoxan, adriamycin and 5-flurouricil (5-FU) with a 16-week regimen (weekly therapy with cytoxan, adriamycin, vincristine, methotrexate, and 5-FU) among women with lymph node positive breast cancer. One hundred sixty-four women participated in the HRQL substudy using the Breast Chemotherapy Questionnaire, which was designed to measure HRQOL in women receiving chemotherapy. Changes in global HRQOL score were examined over time as a predictor of early treatment discontinuation using generalized estimation equations (GEE) modeling and Cox proportional hazards regression. We considered early treatment discontinuation as a longitudinal binary variable determined at each time point HRQOL was measured. The results of multivariate GEE model fitting indicated that declines in HRQOL (p = 0.04), older age (p = 0.02), higher degree of nausea (p = 0.02), higher degree of neurosensory toxicity (0.03) and lower degrees of hair loss (p = 0.004) were correlated with early treatment discontinuation. We then fitted a proportional hazard regression model for time to early discontinuation with HRQOL score as a time-dependent covariate. The results were identical. Declines in HRQOL during therapy predicted early treatment discontinuation even after accounting for age and chemotherapy-related side effects. In the age of ever more aggressive treatments for breast cancer, women's perception of the impact of these treatments on their lives will become more important.

Whelan TJ, Levine M, Julian J, Kirkbride P, Skingley P. The effects of radiation therapy on quality of life of women with breast carcinoma: results of a randomized trial. *Ontario Clinical Oncology Group.* *Cancer.* May 15 2000;88(10):2260-2266. BACKGROUND: The purpose of this study was to evaluate the effect of breast irradiation on quality of life, including cosmetic outcome, for patients enrolled in a clinical trial. METHODS: Between 1984 and 1989, a randomized trial was conducted in Ontario, Canada, in which women with lymph node negative breast carcinoma who had undergone lumpectomy and axillary lymph node dissection were randomized to either breast irradiation or no further treatment. A modified version of the Breast Cancer Chemotherapy Questionnaire (BCQ) was administered to women at baseline, 1 month (4 weeks), and 2 months (8 weeks) after randomization. Irritation of the skin of the breast, breast pain, and appearance of the breast to the patient were also assessed every 3 months for the first 2 years of the study. RESULTS: Of 837 patients, 416 were randomly allocated to radiation therapy and 421 to no further treatment. The mean change in quality of life from baseline to 2 months was -0.05 for the radiation group and +0.30 for the control group. The difference between groups was statistically significant (P = 0.0001). Longer term radiation therapy increased the proportion of patients who were troubled by irritation of the skin of the breast and breast pain. Radiation therapy did not increase the proportion of patients at 2 years who were troubled by the appearance of the treated breast; 4.8% in irradiated and nonirradiated patients (P = 0.62). CONCLUSIONS: Breast irradiation therapy had an effect on quality of life during treatment. After treatment, irradiated patients reported increased breast symptoms compared with controls. However, no difference was detected between groups at 2 years in the rates of skin irritation, breast pain, and being upset by the appearance of the breast.


Calhoun EA, Welshman EE, Chang CH, et al. Psychometric evaluation of the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (Fact/GOG-Ntx) questionnaire for patients receiving systemic chemotherapy. *International Journal of Gynecological Cancer.* Nov-Dec 2003;13(6):741-748. The purpose of this study was to validate the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx) questionnaire. The FACT/GOG-Ntx is the FACT-G plus an eleven-item subscale (Ntx subscale) that evaluates symptoms and concerns associated specifically with chemotherapy-induced neuropathy. Two groups of women with ovarian cancer completed the FACT/GOG-Ntx: one group with known neurotoxicities and one group of chemotherapy-naive women newly diagnosed with ovarian cancer. Levels of patient neuropathy, severity of toxicity, and patient quality of life from diagnosis of ovarian cancer to 12 months post-diagnosis were assessed. The Ntx subscale significantly differentiated the two groups at baseline and 3- and 6-month follow-ups, demonstrating significantly fewer problems among chemotherapy-naive patients than among patients with known neuropathy. The FACT/GOG-Ntx is a reliable
and valid instrument for assessing the impact of neuropathy on health-related quality of life. The Ntx subscale demonstrated sensitivity to meaningful clinical distinctions and change over time.

7. Huang HQ, Brady MF, Cella D, Fleming G. Validation and reduction of FACT/GOG-Ntx subscale for platinum/paclitaxel-induced neurologic symptoms: a gynecologic oncology group study. *International Journal of Gynecological Cancer.* Mar-Apr 2007;17(2):387-393. The FACT/GOG (Gynecologic Oncology Group) Neurotoxicity (Ntx) subscale for assessing platinum/paclitaxel-induced neurologic symptoms was evaluated. The 11-item questionnaire was administered to patients with advanced endometrial cancer treated with doxorubicin/cisplatin (AP) or doxorubicin/cisplatin/paclitaxel (TAP) prior to 1-7 cycles of treatment in GOG 177. The subscale was evaluated in 134 patients in the TAP group for internal reliability, construct validity, criterion validity, sensitivity to treatment differences, and change over time. Cronbach coefficients for internal consistency prior to cycles 1-7 were 0.85, 0.80, 0.84, 0.82, 0.82, 0.85, and 0.84, respectively. The area under the receiver operating characteristic curve was 0.81 for the Ntx score prior to cycle 3. The TAP arm Ntx scores increased significantly from 3.67 at baseline to 8.13 prior to cycle 7; these were higher than the AP arm Ntx scores, which increased from 3.54 at baseline to 4.72 prior to cycle 7. The four sensory items accounted for 80% of treatment differences and 63% of longitudinal changes in the observed subscale score. The 11-item Ntx subscale reliably and validly assesses platinum/paclitaxel-induced peripheral neuropathy. A reduced four-item version is an efficient alternative in measuring this toxicity in clinical trials without compromising its performance.

8. Wenzel LB, Huang HQ, Armstrong DK, et al. Baseline quality of life (QOL) as a predictor of tolerance to intraperitoneal (IP) chemotherapy for advanced epithelial ovarian cancer (EOC): A Gynecologic Oncology Group (GOG) study. *Journal of Clinical Oncology, ASCO Annual Meeting Proceedings.* 2006;24(June 20 Supplement):5007. Background: A recent GOG randomized phase III trial demonstrated a 16 month improvement in survival for women with optimally debulked stage III EOC. Patients on the IP chemotherapy arm experienced a survival advantage but significantly worse toxicities, worse QOL during treatment, and more neurotoxicity (NTX) one year later, compared to those on the IV arm. We sought to determine whether baseline QOL and NTX and abdominal discomfort (AD) predict severity of IP treatment-related adverse effects and number of cycles completed. Methods: Three self-report QOL measures were utilized: the FACT-O (39 items), and FACT/GOG-NTX (11 items) and FACT/GOG-AD (4 items) subscales. Scoring was on a 5-point scale, with higher scores representing better QOL (FACT-O) whereas higher scores indicated worse symptoms (-NTX and -AD subscales). In addition to NTX and AD, we explored associations with fatigue. A logistic regression model was used for the analyses. Results: Of 205 patients randomly assigned to receive IP chemotherapy, 198 (97%) completed baseline QOL assessments, of whom 83 (42%) completed all 6 cycles and 16 (8%) completed none. Adjusting for age, performance status and residual disease, patients reporting higher baseline FACT-O and lower -NTX and -AD scores were more likely to complete more IP cycles. Categorizing FACT-O scores by quartiles (<92, 93 to <108.8, 109 to <121.1, and >121.1), patients in the lowest quartile were significantly less likely to complete 6 cycles of IP therapy (odds ratio [OR] = 4.46; 95% CI: 1.95-10.21, p < 0.001). Higher FACT-O scores were also associated with less grade 3-4 fatigue (OR = 0.81 per 10 points; 95% CI: 0.67-0.99; p = 0.037); however, there was no relationship between baseline NTX and AD subscale scores and severity of physician-rated NTX and AD. Conclusions: Baseline patient-reported QOL and NTX and AD symptoms predict tolerance to IP chemotherapy. Patients with the poorest baseline QOL (FACT-O score <92) were least likely to complete IP therapy.

9. Viala M, Bhakar AL, de la Loge C, et al. Patient-reported outcomes helped predict survival in multiple myeloma using partial least squares analysis. *Journal of Clinical Epidemiology.* Jul 2007;60(7):670-679. OBJECTIVE: The prognostic value of Patient-Reported Outcomes (PRO) in predicting mortality during treatment of multiple myeloma (MM) patients was assessed using partial least square (PLS) regression, a statistical method that is well-adapted for highly correlated data. STUDY DESIGN AND SETTING: Four PRO measures, The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, the EORTC QLQ-MY24, the FACIT-Fatigue scale, and the FACT/GOG-Ntx scale, were administered during a trial designed to evaluate the efficacy and safety of bortezomib (VELCADE 1.3mg/m(2)) in MM patients (N=202). Clinical and PRO data were analyzed for predictive value by univariate and multivariate logistic regression methods and then by PLS regression. RESULTS: Fifteen baseline PRO parameters were significant in predicting mortality during treatment when univariate logistic regression was used. In contrast, only two variables were retained in the multivariate analysis, as correlated variables were excluded from the model. Using PLS regression, 14 of the 21 PRO predictors were significant in predicting mortality. Clinical and PRO data used together increased the predictive
power of all models compared to clinical data alone. CONCLUSION: The prognostic value of PRO was established and was more informative using PLS regression. PLS regression may therefore be a valuable method for analyzing PRO data.

10. Richardson PG, Briemberg H, Jagannath S, et al. Frequency, characteristics, and reversibility of peripheral neuropathy during treatment of advanced multiple myeloma with bortezomib. *Journal of Clinical Oncology.* Jul 1 2006;24(19):3113-3120 PURPOSE: To determine the frequency, characteristics, and reversibility of peripheral neuropathy from bortezomib treatment of advanced multiple myeloma. PATIENTS AND METHODS: Peripheral neuropathy was assessed in two phase II studies in 256 patients with relapsed and/or refractory myeloma treated with bortezomib 1.0 or 1.3 mg/m2 intravenous bolus on days 1, 4, 8, and 11, every 21 days, for up to eight cycles. Peripheral neuropathy was evaluated at baseline, during the study, and after the study by patient-reported symptoms using the Functional Assessment of Cancer Therapy Scale/Gynecologic Oncology Group–Neurotoxicity (FACT/GOG-Ntx) questionnaire and neurologic examination. During the study, peripheral neuropathy was also evaluated by investigator assessment. A subset of patients underwent nerve conduction studies (n = 13). RESULTS: Before treatment, 194 (81%) of 239 patients had peripheral neuropathy by FACT/GOG-Ntx questionnaire, and 203 (83%) of 244 patients had peripheral neuropathy by neurologic examination. Treatment-emergent neuropathy was reported in 35% of patients, including 37% (84 of 228 patients) receiving bortezomib 1.3 mg/m2 and 21% (six of 28 patients) receiving bortezomib 1.0 mg/m2. Grade 1 or 2, 3, and 4 neuropathy occurred in 22%, 13%, and 0.4% of patients, respectively. The incidence of grade > or = 3 neuropathy was higher among patients with baseline neuropathy by FACT/GOG-Ntx questionnaire compared with patients without baseline neuropathy (14% v 4%, respectively). In all 256 patients, neuropathy led to dose reduction in 12% and discontinuation in 5%. Of 35 patients with neuropathy > or = grade 3 and/or requiring discontinuation, resolution to baseline or improvement occurred in 71%. CONCLUSION: Bortezomib-associated peripheral neuropathy seemed reversible in the majority of patients after dose reduction or discontinuation. Although severe neuropathy was more frequent in the presence of baseline neuropathy, the overall occurrence was independent of baseline neuropathy or type of prior therapy.

11. Cella D, Peterman A, Hudgens S, Webster K, Socinski MA. Measuring the side effects of taxane therapy in oncology: the functional assessment of cancer therapy-taxane (FACT-taxane). *Cancer.* Aug 15 2003;98(4):822-831 BACKGROUND: Cancer chemotherapy with some of the taxane class of agents can be associated with significant neurotoxicity, arthralgias, myalgias, and skin changes that may offset the therapeutic benefits of taxane use. METHODS: The authors developed and tested a set of questions to assess these important side effects of taxane therapy from the patient’s perspective. The current study evaluated the taxane subscale of the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system. Reliability, validity, and responsiveness to expected change were evaluated in the context of an ongoing clinical trial comparing four cycles of carboplatin plus paclitaxel with a strategy of carboplatin plus paclitaxel until disease progression in patients with advanced nonsmall cell lung carcinoma (NSCLC). RESULTS: The 16-item Taxane subscale score and the 11-item peripheral neuropathy subset both demonstrated excellent internal consistency and concurrent validity, and the scores worsened as one would predict during a 12-week treatment course of taxane therapy. Results of the psychometric analyses supported the use of this subscale for measuring the unwanted adverse consequences of effective cancer therapies. Measuring the patient perception of treatment side effects also allowed a preliminary exploration of the relative quality of life (QOL) impact of symptom relief and treatment toxicity. The results indicated that toxicity and symptom improvement may make relatively equivalent contributions to total QOL as measured by the summary score from a multidimensional QOL instrument, the Functional Assessment of Cancer Therapy-General. However, symptom status and improvement appear to play a stronger role than taxane toxicity in patients’ global rating of their QOL. CONCLUSIONS: Future research might examine this question of competing benefits as a potential aid to decision-making regarding the administration of toxic therapies in the setting of advanced disease. Copyright 2003 American Cancer Society.

12. Wenzel LB, Huang HQ, Armstrong DK, Walker JL, Cella D, Gynecologic Oncology G. Health-related quality of life during and after intraperitoneal versus intravenous chemotherapy for optimally debulked ovarian cancer: a Gynecologic Oncology Group Study. *Journal of Clinical Oncology.* Feb 1 2007;25(4):437-443 PURPOSE: A Gynecologic Oncology Group (GOG) randomized phase III trial (GOG 172) in optimal stage III epithelial ovarian cancer showed that intravenous (IV) paclitaxel plus intraperitoneal (IP) cisplatin and paclitaxel significantly lengthened progression-free survival and overall survival compared with IV paclitaxel and cisplatin. The purpose of this report is to comprehensively evaluate the patient-
reported outcomes associated with IP versus IV therapy. PATIENTS AND METHODS: Four hundred fifteen eligible women were enrolled onto GOG 172 at member institutions. The Functional Assessment of Cancer Therapy-Trial Outcome Index (FACT-TOI; which includes physical, functional, and ovarian subscales) and neurotoxicity (Ntx) and abdominal discomfort (AD) subscales were used to assess patient-reported outcomes. Assessments were completed before random assignment, before cycle 4, and 3 to 6 weeks and 12 months after treatment. RESULTS: Physical and functional well-being and ovarian cancer symptoms were significantly worse in the IP arm before cycle 4 (P < .001) and 3 to 6 weeks after treatment (P = .001 for FACT-TOI). Patients in the IP arm also reported significantly worse AD before cycle 4 (P < .001) and significantly worse Ntx 3 to 6 weeks (P = .001) and 12 months (P = .003) after completing IP treatment. In general, however, the quality of life of both groups improved over time. CONCLUSION: During active treatment, patients on the IP arm experienced more health-related quality-of-life disruption, AD, and Ntx compared with patients receiving conventional IV therapy. However, only Ntx remained significantly greater for IP patients 12 months after treatment. This trade-off should be included when discussing treatment options with patients. Future studies to mitigate the added burden associated with IP therapy are planned.


BACKGROUND: The optimal schedule of taxane administration has been an area of active interest in several recent clinical trials. METHODS: To address a pure schedule question, we randomized 161 patients with advanced stage IIIB or IV non-small-cell lung cancer (NSCLC) to either paclitaxel 225 mg/m2 every 3 weeks x 4 cycles or 75 mg/m2/week x 12 (cumulative dose on each arm = 900 mg/m2). Both arms received concurrent carboplatin AUC 6 every 3 weeks x 4 cycles. RESULTS: The two arms were well-balanced in terms of known prognostic factors. The overall response rate and survival outcomes were similar on the two arms. There was significantly more grade 3/4 thrombocytopenia and grade 2-4 anemia on the weekly arm but less severe myalgias/arthritis and alopecia. No difference in the rates of peripheral neuropathy was observed; however, patients on the every 3 weeks arm reported significantly more taxane therapy-related side-effects on the functional assessment of cancer therapy taxane subscale. CONCLUSIONS: This randomized trial exploring schedule-related issues with carboplatin/paclitaxel confirms the versatility of this regimen.


In previous studies of the side effects patients identified as important in cancer chemotherapy we identified eight groups of symptoms. Linear analogue self assessment (LASA) scales for these 8 items form a new instrument (GLQ-8) for measuring aspects of quality of life. Patients completed both GLQ-8 and five previously validated LASA scales, together with a new single global quality of life scale (GLQ uniscale) and the visual analogue version of the Spitzer QL Index. This analysis includes 166 patients, with 47 1-hr test-retest and 29 24-hr test-retest pairs. The new scales showed high reliability, with retest correlation coefficients exceeding 0.8 for all items except GLQ uniscale, appetite and anxiety on 1-hour retest, and all except nausea and numbness on 24-hour retest. Correlations were in general higher for the GLQ-8 items than for the 5 older LASA items, while inter-item correlations were lower. Comparisons of the new scales with established instruments and comparisons of new scale scores between known groups supported the validity of the new scales. We conclude that the GLQ-8 and GLQ uniscale are convenient and reliable instruments measuring aspects of quality of life in patients receiving cancer chemotherapy.


Four measures of patient functioning and a mood adjective list currently used in trials of the International Breast Cancer Study Group (IBCSG), and an 8-item Linear Analogue Self Assessment (LASA) instrument measuring specific side effects of cancer and cancer treatment (GLQ-8), were cross-validated against three established measures of quality of life, mood and psychological adjustment to cancer, in a heterogeneous sample of cancer patients. Correlations between new and established measures were high, indicating good convergent and concurrent validity. Compliance on the longer mood measures was relatively poor. Despite the difficulty in developing direct and methodologically sound measures of quality of life, the regular inclusion of practical indicators of aspects of quality of life in clinical trials would allow improved assessment of the cost-benefit ratio of treatment to outcome in cancer patients.
16. Coates A, Thomson D, McLeod GR, et al. Prognostic value of quality of life scores in a trial of chemotherapy with or without interferon in patients with metastatic malignant melanoma.[see comment]. European Journal of Cancer. 1993;29A(12):1731-1734 In a multi-centre randomised clinical trial comparing dacarbazine (DTIC) plus recombinant interferon-alfa2a (IFN) versus DTIC alone for patients with metastatic malignant melanoma, aspects of quality of life (QL) were measured prospectively by patients using linear analogue self assessment (LASA) scales including the GLQ-8 and by doctors using Spitzer's QL Index. QL scores and performance status at the time of randomisation were available for 152 of 170 eligible patients. These scores carried significant prognostic information. In univariate analyses, Spitzer QL Index assessed by the doctor and LASA scales for physical wellbeing (PWB), mood, pain, appetite, nausea and vomiting, GLQ-8 total and overall QL were significant (P < 0.01) predictors of subsequent survival. QL Index and LASA scales for mood, appetite, and overall QL remained independently significant (all P < 0.05) in multivariate models allowing for significant prognostic factors other than QL (liver metastases and performance status). These findings closely parallel those in patients with metastatic breast cancer. They add further validity to the QL Index and LASA scores, provide the first evidence of the prognostic significance of the GLQ-8, and argue strongly for the routine assessment of QL in future therapy trials.

17. Butow PN, Coates AS, Dunn SM. Psychosocial predictors of survival in metastatic melanoma.[see comment]. Journal of Clinical Oncology. Jul 1999;17(7):2256-2263 PURPOSE: Research interest in psychosocial predictors of the onset and course of cancer has been active since the 1950s. However, results have been contradictory and the literature is noted for methodologic weaknesses. In this prospective study, we aimed to systematically obtain data on psychosocial factors associated with human response to illness. PATIENTS AND METHODS: One hundred twenty-five patients with metastatic melanoma completed questionnaires measuring cognitive appraisal of threat, coping, psychologic adjustment, perceived aim of treatment, social support, and quality of life (QOL). Questionnaires were completed, where possible, every 3 months for 2 years after diagnosis. Survival was measured from date of study entry to date of death or was censored at the date of last follow-up for surviving patients. RESULTS: In a multivariate Cox regression analysis of baseline data, which controlled for demographic and disease predictors, the psychologic variables of perceived aim of treatment (P <.001), minimization (P <.05), and anger (P <.05) were independently predictive of survival. Patients who were married (P <.01) and who reported a better QOL (P <.05) also survived longer. CONCLUSION: The prognostic significance of psychologic and QOL scores remained after allowance for conventional prognostic factors. If these associations reflect an early perception by the patient or doctor of disease progression, then measures are at least valuable early indicators of such progression. If psychologic processes have a more direct influence on the course of the underlying illness, then it may be possible to manipulate them for therapeutic effect. We are now conducting a randomized controlled trial of a psychologic intervention to further elucidate these issues.

18. Semiglasov VF, Stepula VV, Dudov A, Lehmacher W, Mengs U. The standardised mistletoe extract PS76A2 improves QoL in patients with breast cancer receiving adjuvant CMF chemotherapy: a randomised, placebo-controlled, double-blind, multicentre clinical trial. Anticancer Research. Mar-Apr 2004;24(2C):1293-1302 Patients with breast cancer receiving adjuvant chemotherapy frequently suffer from a restricted quality of life (QoL) due to the side-effects of chemotherapy and the consequences of coping with the diagnosis. Therefore, the objective of this clinical study was to investigate the impact of PS76A2, an aqueous mistletoe extract standardised to the galactoside-specific mistletoe lectin, on QoL by performing a placebo-controlled trial. Overall, 272 patients with breast cancer receiving adjuvant CMF chemotherapy (cyclophosphamide-methotrexate-fluorouracil) were enrolled and randomised to groups receiving placebo or PS76A2 at concentrations of 10, 30 or 70 ng mistletoe lectin (ML) per ml. The patients received 0.5 ml study medication twice weekly subcutaneously for 15 consecutive weeks (4 CMF cycles). Primary variables were the self-assessment QoL scores GLQ-8 (Global Life Quality) and Spitzer's uniscale. As a result, statistically significant effects on QoL were obtained with the medium dose (15 ng ML/0.5 ml). The treatment difference between the medium dose and placebo with regard to the GLQ-8 sum was 60.8 mm (95% confidence interval: 19.3 to 102.0 mm). The treatment effect for Spitzer's uniscale between the medium dose and placebo was 16.4 mm (95% confidence interval: 6.3 to 26.6 mm). The results on QoL were supported by an increase of T helper lymphocytes (CD4+) and the CD4+/CD8+ ratio (p<0.05). Overall, PS76A2 was well tolerated. Local reactions at the injection sites occurred dose-dependently, but were mild at the low and medium dose levels.

characteristics of two indexes used to evaluate the subjective morbidity of chemotherapy regimens were analyzed. Both indexes assessed the duration of discomfort as perceived by the patient throughout therapy. The first index asked patients to state the number of days spent with 'discomfort', and the second index asked them which days they would like to eliminate altogether because of the unbearable symptoms experienced on those days. While the first index gives some idea of the duration of suffering, without defining it, the second highlights a specific time when the quality of her life was unacceptable to the patient. We studied these indexes in the form of a questionnaire completed by 168 women who had entered a cancer clinical trial. This trial evaluated the efficacy of primary chemotherapy in rendering conservative surgery feasible in women with operable breast cancer, but whose tumor size was greater than 3 cm. Four different treatment regimens were used: CMF, FAC, FEC, FNC (C = cyclophosphamide, M = methotrexate, F = fluorouracil, A = adriamycin, E = epirubicin, N = mitoxantrone). Seventy-nine patients were interviewed during chemotherapy and 89 during follow-up visits. Initial assessment of the reliability, discriminant and concurrent validity of the two indexes produced satisfactory results. Finally, we analyzed the responses given by 168 patients for a total of 600 treatment cycles. The average value of 'discomfort' was 3 days, whereas the average value of days 'to be eliminated' was 1. The range of subjective morbidity (for every cycle of treatment: 'discomfort = 0-30 days; 'to be eliminated' = 0-20 days) was very broad.(ABSTRACT TRUNCATED AT 250 WORDS).

20. Sitzia J, Dikken C, Hughes J. Psychometric evaluation of a questionnaire to document side-effects of chemotherapy. Journal of Advanced Nursing. May 1997;25(5):999-1007 This paper reports the psychometric testing of the Worthing Chemotherapy Questionnaire (WCQ). The WCQ is a patient self-report instrument to document side-effects of chemotherapy. Literature review of relevant studies shows that psychometric testing of similar instruments is rarely rigorous. Content validity for the WCQ was established in five ways: literature review, Delphi review among oncology staff, pre-pilot unstructured interviews, pilot study and amendment of the instrument and items for spontaneous reporting of problems on the questionnaire. A three-stage approach to construct validity was used. The hypothesis adopted was that as certain cytotoxic agents cause stomatitis, incidence and severity of stomatitis will decrease following cessation of treatment. Stage 1: factor analysis confirmed the presence of a sole factor, with an eigenvalue of 5.3, for mouth problems which explained 65.5% of the variance. Stage 2: the hypothesis was confirmed using research findings. Stage 3: the Wilcoxon test showed highly significant results for during and post chemotherapy stomatitis scores. Reliability of the questionnaire was assessed using the test-retest method. Weighted kappa was chosen as the test statistic. A median value of wk = 0.87 was obtained. The results indicate that the WCQ is a reliable and valid instrument.

21. Buckingham R, Fitt J, Sitzia J. Patients’ experiences of chemotherapy: side-effects of carboplatin in the treatment of carcinoma of the ovary. European Journal of Cancer Care. Mar 1997;6(1):59-71 There has been little investigation of the side-effects experienced by women receiving adjuvant carboplatin in the treatment of ovarian cancer. This study aimed to describe the range of problems experienced by patients and to estimate incidence and severity of side-effects over the treatment period. Eleven patients participated and completed a 75-item self-report questionnaire at each course of treatment. Severity of each side-effect was graded from 0 to 4. Patients also stated which had been the worst side effect at each course. The response rate was 94%. Seventy-two side-effects were reported. Fatigue emerged as both the most common and the most ‘troublesome’ side-effect. Nausea, difficulty sleeping, taste change, and constipation were also ranked highly. Although limited by a small sample size, this study suggests patients undergoing carboplatin experience a wide range of problems, many of which merit further investigation.