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Paclitaxel-based high-dose chemotherapy with autologous stem cell rescue for relapsed germ cell tumor: Clinical outcome and quality of life in long-term survivors

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Abstract

Background—High dose chemotherapy (HDCT) is a viable and potentially curative approach for patients with relapsed or refractory germ cell tumors (GCTs). However, no comparative data exist to define the optimal chemotherapeutic strategy, and little is known about the quality of life (QOL) of long-term survivors. Herein, we attempt to characterize the QOL in long-term survivors in patients receiving high-dose paclitaxel, etoposide, carboplatin and ifosfamide (TECTIC).

Methods—Details of the TECTIC regimen and clinical outcomes for the initial 33 patients have been reported. In the present study, we report the clinical data for 15 additional patients. Using the EORTC QLQ-C30 and the FACT-T questionnaires, we surveyed all patients who survived at least 4 years after HDCT.

Results—Forty-eight patients were enrolled and 46 patients received protocol therapy. For all 48 patients, the median progression-free survival (PFS) and overall survival (OS) were 11.8 months (range, 5.8-NR) and 21.7 months (range, 12.7-NR), respectively. Seventeen patients were progression-free at a median of 123.2 months (51.6-170.2), and 6 patients remain alive following progression with a median OS of 68.8 months (47.6-147.1). Of the 23 surviving patients, 18 were accessible and consented to telephonic interview. As compared to historical cohorts (Rossen *J Clin Oncol* 2009), survivors had a higher global health scale score (87.04 v 75.62; P=0.02) but a lower physical functioning score (68.89 v 92.66; P=0.0001) by the QLQ-C30 scale.

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Conclusions—HDCT with the TECTIC regimen produces durable remissions in patients with relapsed or refractory GCTs with acceptable QOL in long-term survivors.

Keywords

TECTIC; paclitaxel; high dose chemotherapy; autologous transplant; testicular cancer; quality of life; germ cell tumors

INTRODUCTION

For nearly three decades, cisplatin-based chemotherapy has represented the cornerstone of first-line treatment for patients with advanced germ-cell tumors.(1) In unselected patients, complete response (CR) rates in the range of 70-80% can be achieved.(2) Although there is little debate regarding the utility of this strategy, there is some degree of equipoise in selecting salvage approaches for patients with relapsed or refractory disease. Current guidelines suggest consideration of either high-dose chemotherapy (HDCT) or salvage conventional-dose chemotherapy (CDCT) in those with a favorable prognosis, defined by features including low serum tumor markers, low net tumor, a CR to first-line chemotherapy and/or a testicular primary.(3) A retrospective analysis of HDCT with carboplatin and etoposide followed by autologous hematopoietic cell rescue suggested long-term disease-free survival (DFS) in nearly 70% of patients receiving the regimen as second-line therapy (notably, most patients received 2 cycles of HDCT).(4) Potential CDCT options in patients in first relapse generally consist of 3-drug combinations containing cisplatin, vinblastine or etoposide, ifosfamide and paclitaxel. The probability of favorable outcomes, generally defined as continuous complete remissions at 2 years (relapses are rare after 2 years), appears to depend more on patient prognostic characteristics than on identifiable treatment factors.(5-7)

There remains a relative paucity of data to directly compare the overall risks and benefits of CDCT with those of HDCT in the treatment of relapsed GCT. Recently, Lorch *et al* analyzed patients in an international database derived from 1,984 patients with germ cell tumors (GCTs) that had progressed after at least 3 cycles of cisplatin-based combination chemotherapy. Among these patients, 773 patients received CDCT only for the treatment of relapse, while 821 patients received HDCT as a component of treatment for first relapse.(8) The hazard ratio (HR) for overall survival (OS) among patients unselected by prognostic category was 0.65 (95%CI, 0.56-0.75), favoring HDCT. Among the 5 prognostic subgroups, all but one showed a favorable effect of HDCT (patients in the low-risk subset had similar outcomes with CDCT or HDCT. With limited prospective evidence to guide the oncologist, these data have been used to provide the rationale for continuing to offer HDCT in an attempt at curative second-line therapy for patients with relapsed GCT.

In recent years, several HDCT strategies have been assessed. For instance, a regimen of paclitaxel and ifosfamide followed by high-dose carboplatin and etoposide (TI-CE) has been assessed by the MSKCC group, with a reported 5-year disease-free survival (DFS) of 47% and OS of 52%.(9) This regimen may soon be evaluated in a prospective, phase III study comparing HDCT and CDCT as second-line therapy. Recognizing the high activity of paclitaxel-based regimens for relapsed GCT and their relatively favorable acute therapeutic index, we studied tandem HDCT cycles using nonidentical paclitaxel-based combinations (with etoposide and carboplatin in cycle 1 and with ifosfamide and carboplatin in cycle 2) and showed favorable tolerance and disease outcomes in an initial cohort of 33 patients.(10) We then treated additional patients in order to obtain more data and to enrich our patient population for the most unfavorable prognostic factors, such as relapsed mediastinal GCT. While the heterogeneity of patient populations and treatment variables precludes any type of

comparison, we were encouraged by observing outcomes (approximately 40% durable CR) similar to those of the MSKCC group using TI-CE. We report here the longer-term follow-up of our original cohort as well as the data for the 15 additional patients.

To date, there are no head-to-head comparisons of HDCT strategies for relapsed and refractory GCTs. As such, the oncologist is challenged with juxtaposing the safety and efficacy of distinct regimens, reflected in independent datasets. Given the potential for long-term survival, health related-quality of life (HR-QOL) and the risk of incurring comorbid illnesses is also of prime importance. There is little data to this effect in this patient population. Rossen *et al* have recently reported data pertaining to the HR-QOL of 401 patients with GCTs of varying stage. Notably, these patients had received a heterogeneous array of treatment modalities – only 150 patients (35%) had been previously treated with chemotherapy.(11) Those patients receiving chemotherapy did have higher levels of specific toxicities (peripheral sensory neuropathy, ototoxicity, and Raynaud-like phenomena), but did not have a substantial difference in HRQOL as compared to non-cancer patients. Although these data are useful in guiding efforts to assess psychosocial parameters in patients with GCTs, the HR-QOL of patients with relapsed and refractory disease cannot be inferred from this work. Recent studies have also highlighted an increased risk of cardiovascular co-morbidity in patients receiving conventional first-line therapies (i.e., bleomycin, etoposide and cisplatin). Akin to the previous dilemma, there is little comparable data to suggest the long-term risks associated with salvage approaches.

Herein, we report extended follow-up data associated with our experience assessing high-dose paclitaxel, carboplatin, ifosfamide and etoposide (TECTIC) followed by autologous peripheral stem cell transplant (aPSCT) in patients with relapsed and refractory GCTs. We further provide an assessment of HR-QOL and cardiovascular morbidity in long-term survivors treated on this protocol.

METHODS

Patients and Treatment Protocol

Eligibility criteria for the current study have been previously published, along with details of the treatment protocol. Briefly, eligible patients received stem cell mobilization with granulocyte-colony stimulating factor (G-CSF) at 10 µg/kg/d subcutaneously prior to leukapheresis. G-CSF administration was continued daily during collection until the total collected product excelled 4×10^6 CD34⁺ cells/kg. Patients received a 24-hour intravenous (IV) infusion of paclitaxel at 350 mg/m² (first 5 patients) or 425 mg/m² (all other patients) on day -7. Subsequent to this, patients received etoposide (20 mg/kg IV over 2 hours) and carboplatin (area under the curve, AUC, of 7 mg-min/mL IV over 30 minutes) daily on days -6, -5 and -4. Patients received an IV infusion of 12.5% of the derived CD34⁺ stem cell product on day -2, followed by administration of 37.5% of the product on day 0. Patients who had recovered from acute toxicities and had no demonstrable evidence of progression were permitted to proceed to cycle 2, comprised of paclitaxel, ifosfamide and carboplatin. Ifosfamide was administered IV daily at 3 g/m² over 30 minutes on days -6, -5 and -4. Mesna was administered 24 hours subsequently as a 1 g/m² bolus dose followed by 10g/m² via continuous IV infusion over 72 hours. The derived CD34⁺ stem cell product was administered in a manner identical to that during Cycle 1 on days -2 and 0. Clinical and data monitoring are described in the original manuscript as well. Notably, a schedule for clinical, laboratory and radiographic examinations was specified until 5 years after treatment, after which point follow-up was at the discretion of the treating physician.

As in the previous publication, patients were risk stratified using International Germ Cell Cancer Collaborative Group (IGCCCG) criteria and by Beyer score.(12-13) Notably,

designation of the IGCCCG risk stratification was based on clinicopathologic characteristics at the time of initial diagnosis with GCT.

Quality of Life Survey

Follow-up survey data were collected via telephonic interview through an IRB-approved protocol amendment. All surveys were conducted by a single co-investigator (S.K.P.). The European Organization for the Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire (version 3.0) was administered to accessible survivors. The QLQ-C30 is a validated instrument used to evaluate HR-QOL in patients with cancer, and assesses symptoms (fatigue, nausea, vomiting, and pain), functional domains (physical, cognitive, emotional, and social), and other symptoms encountered frequently in cancer patients (dyspnea, insomnia, constipation, diarrhea and loss of appetite).(14) The perceived financial impact of cancer treatment and outcome is also assessed. Responses were collected on a Likert scale (rated from 1 [very poor] to 7 [excellent]), akin to the remainder of the questionnaire. A full version of the QLQ-C30 questionnaire is available at <http://www.eortc.be/home/qol>.

To assess the specific toxicities associated with high-dose paclitaxel chemotherapy (a unique component of the current treatment protocol), the Functional Assessment of Cancer Therapy-Taxane (FACT-Taxane) scale was utilized. The FACT-Taxane scale is a validated instrument that contains specific questions addressing neuropathy, arthralgias, tinnitus, edema and other taxane specific symptoms.(15) Responses are graded on a 5-point Likert scale.(15) A full version of the FACT-Taxane questionnaire is available at <http://www.facit.org>.

Cardiovascular Comorbidity

As reported by Haugnes *et al*, long-term survivors of chemotherapy may have an increased risk of cardiovascular complications resulting from the “metabolic syndrome” of diabetes, hypertension and hyperlipidemia. Therefore, we also queried patients regarding a diagnosis (prior to or after HDCT) of diabetes, use of an antihypertensive agent, or use of a lipid-lowering agent. Patients provided their most recent height and weight for calculation of body-mass index (BMI). Obesity was defined as a BMI ≥ 30 kg/m².

Statistical Methods

Median progression-free survival (PFS) and OS were computed for the intent-to-treat population. PFS and OS were determined from the time of protocol-based procedures to the time of tumor marker progression and death, respectively. Standard Kaplan-Meier methods were employed for these analysis using S-plus software (S-Plus 6.0; Insight-ful, Seattle, WA). Significance testing was 2-sided. A mean score for each of the domains of the QLQ-C30 questionnaire was determined. A two-sample student's t-test was used to compare the individual and cumulative mean values to those reported by Rossen *et al* for a cohort of 150 patients with varying stages of germ cell tumor receiving chemotherapy.(11) For the additional two items generated to supplement the QLQ-C30 questionnaire, descriptive statistics were applied to these items. The mean FACT-Taxane score was computed, and a two-sample student's t-test was used to compare cumulative mean scores to those reported by Cella *et al* for a cohort of 230 patients receiving conventional doses of paclitaxel for non-small cell lung carcinoma (NSCLC). The frequency of diabetes, use of lipid-lowering agents, and use of antihypertensive agents was computed, with annotation for onset prior to or after HDCT.

RESULTS

Clinical Outcomes

From February of 1997 to May of 2007, 48 patients were consented and enrolled. Two patients did not receive protocol therapy due to rapidly progressing disease during preparative workup but are included in the denominator for survival analyses by the principle of intent to treat. Characteristics of the population are noted in Table 1. Forty-three patients (91.5%) had non-seminomatous histology. In our updated cohort, 17 patients did not proceed to the second cycle of high-dose therapy, 11 due to progressive disease. Of the remaining 6 patients, 5 had toxicities precluding the second cycle (2 patients with neuropathy, 2 patients with cardiac issues, and 1 patient with mucositis), and one additional patient (a heavy smoker) developed a severe fungal pulmonary infection after the first cycle of high-dose therapy. The median time between administration of cycle 1 and 2 of high-dose therapy was 51 days (range, 41-79). Median PFS for the overall cohort was 11.8 months (range, 5.8-NR), and median OS was 21.7 months (range, 12.7-NR) (Figure 1). When stratified by Beyer score, patients with intermediate risk disease had a substantial improvement in PFS as compared to patients with poor risk disease (median PFS 25.7 months *v* 1.8 months, *p*=0.005) (Figure 2). Similarly, OS was improved in those patients with intermediate risk disease (median OS not reached *v* median OS 9.3 months, *p*=0.005). In contrast, no statistically significant difference in PFS or OS was seen in groups stratified by IGCCCG risk group by any grouping of risk categories.

In the overall cohort, a total of 17 patients were alive and progression free at a median of 123.2 months (range 51.6-170.2). Twenty-five (25) patients died, one from infection (<1 month), 1 from cardiac arrest (17.7 months), and 23 from progressive tumor. Six patients are alive after disease progression with a median overall survival of 68.8 months (range 47.6-147.1). The most frequent grade 3/4 toxicities during cycle 1 were mucositis/stomatitis, hyperglycemia, transaminitis, and nausea/vomiting, as delineated in Table 2. During cycle 1, one patient experience grade 5 infection and grade 5 pulmonary infiltrations in association with grade 4 renal failure. Although the frequency of grade 3/4 toxicities decreased during cycle 2 of therapy, a similar spectrum of toxicities was observed.

Toxicity

QLQ-C30 Assessment—Of 23 patients who are currently alive after receiving protocol-based therapy (verified by consultation with treating oncologists and review of data from the Social Security Death Indices), 18 patients were accessible for telephonic interview (5 patients did not return phone calls; no patients refused consent). All patients offered verbal consent to participate in the analyses prior to assessment. A median of 115.6 months (range, 38.9-185.9 months) elapsed from the time of enrollment to the time of survey administration. Average scores and association standard deviations for all components of the QLQ-C30 are denoted in Table 3, along with corresponding values from a cohort of 150 patients with GCT who received chemotherapy, as reported by Rossen *et al.* In comparison to this cohort, two significant differences were identified. First, patients in the current cohort had a higher global health scale score (87.04 *v* 75.62; *P*=0.02). Second, patients in the current cohort had a lower physical functioning score (68.89 *v* 92.66; *P*=0.0001). A summary score of 82.41 (SD, 32.6) was determined in a manner analogous to that for the other domains of the QLQ-C30 tool.

FACT-Taxane Assessment—The FACT-Taxane tool was used to assess the same cohort of 18 patients. A mean score of 56.60 (SD, 13.24) was calculated. A limited array of datasets have employed the FACT-Taxane scale to date. Cella *et al* performed an initial validation of the tool in a cohort of 143 patients receiving conventional doses of taxane

chemotherapy for NSCLC; this cohort was used as a comparator in the current study (see Table 4). No difference was observed in a comparison of FACT-Taxane scores for patients in the current study to the baseline and 6-week scores of patients with NSCLC ($P=0.16$ and $P=0.93$, respectively). However, FACT-Taxane scores for patients in the current study were higher than those for patients assessed by Cella *et al*/who had been treated with 12-weeks of conventional taxane therapy.

Co-morbidity—Four of the 18 patients (22%) reported a diagnosis of diabetes, 3 occurring after HDCT. Three patients (17%) reported current use of antihypertensive medications, and 4 patients (22%) were taking lipid-lowering agents, all started after HDCT. The average BMI in the cohort was 30.3 (SD, 7.9).

DISCUSSION

The data presented herein suggests the potential for durable survival in association with TECTIC chemotherapy, with 17 patients, or 35% of the examined cohort, alive at a median follow-up of 123 months. OS was improved in those patients with intermediate-risk as defined by Beyer score; notably, no significant difference in survival was seen in groups stratified by IGCCCG score. The regimen is not without appreciable toxicity, with notable side effects including mucositis/stomatitis, hyperglycemia, transaminitis, and nausea/vomiting. Nonetheless, our survey analyses do suggest that a reasonable QOL can be maintained in long-term survivors. HDCT with the TECTIC regimen followed by ASCT is therefore a potential therapeutic strategy for relapsed or refractory GCTs.

The optimal strategy in this setting has yet to be determined. As previously noted, Lorch *et al*/have published a detailed account of survival in 1,984 patients who received conventional dose or HDCT for relapsed or refractory GCTs, with a compelling suggestion of OS benefit in patients receiving HDCT.(8) Although the authors took the important step of stratifying by prognostic group, retrospective analyses such as these are inherently challenged by the selection bias that occurs in identifying patients appropriate for stem cell transplantation. In the Eastern Cooperative Oncology Group (ECOG), plans are underway for a phase III clinical trial that will compare the aforementioned TI-CE regimen (in association with ASCT) to 4 cycles of conventional dose chemotherapy with paclitaxel, ifosfamide and cisplatin (TIP).(16) However, such studies will take many years to mature, and in the interim, clinicians will be faced with the quandary of interpreting the relative benefit of each treatment approach.

Limitations of the current study include a lack of existing QOL data to generate optimal comparisons. The Germinative Tumor Database (GTD) was used by Rossen *et al*/to identify a total of 695 patients treated between 1990 and 1999 for male GCTs. One hundred fifty of those patients received various chemotherapies but due to differences in the chemotherapy and the followup time compared to our study as well as patient characteristics favoring those in the Rossen report, it is not feasible to make direct comparisons. Nonetheless, we believe that the higher scores calculated for our patients on the QLQ-C30 global health survey suggest that the paclitaxel-based tandem HDCT regimens we used are associated with a very acceptable long-term post-HDCT global QOL. Another caveat of our study design was the use of telephonic surveys. While telephonic surveys allow for rapid obtainment of relevant data, there are several biases that this mode of data collection may introduce. First, a “response bias” may exist – respondents may find it challenging to relay sensitive information over the telephone. Our inquiries ranged from objective questions regarding physical parameters (i.e., height and weight) to very sensitive questions regarding emotional well-being. While respondents may have had little difficulty divulging such information in a less personal paper format, they may have balked at conveying this information directly to a

human interviewer. This phenomenon is well documented, particularly in the setting of surveys for drug and alcohol abuse.(17) A second form of bias is “coverage bias”, referring to the fact that telephonic surveys may exclude homeless individuals, or those without current possession of a telephone. Again, several examples of this abound in the psychiatric literature.(18) Outside of the issues with the telephonic survey design, our study is also susceptible to “recall bias” – since our surveys took place at a substantial length of time following the treatment intervention, it may be challenging to report the relationship of adverse events with the intervention. This may be of particular concern in our reporting of diabetes, antihypertensive use, and lipid-lowering agent use (since we inquired about the time of onset of these symptoms). The challenge we encountered in ascertaining these variables underscore the need to employ appropriate long-term follow-up of GCT patients.

Neuropathy, of particular concern with a paclitaxel-based regimen, was substantial with the first cycle of high-dose therapy (10 of 46 patients, or 22%, had grade 3/4 toxicity), but was less prevalent with the second cycle (grade 3/4 toxicity was not observed). This observation may reflect attrition of patients who suffered more substantial toxicity between the first and second cycles of high-dose therapy. With respect to our assessment of FACT-Taxane scores, to our knowledge, this metric has not been previously used to assess patients with either primary or relapsed/refractory GCTs. As such, we utilized a cohort of patients with NSCLC reported by Cella *et al* to make some indirect comparisons and inferences. While patients in the current study may have received taxane therapy upwards of 10 years ago, patients in the comparator group were prospectively assessed at baseline and at 6- and 12-weeks of taxane treatment. The FACT-Taxane yielded at 6- and 12-weeks may be more reflective of acute toxicities related to these agents. Furthermore, it is unclear whether disease-related characteristics may influence the FACT-Taxane score. These limitations notwithstanding, it was encouraging that FACT-Taxane scores in our cohort were not dissimilar from FACT-Taxane scores at baseline in the comparison group. These findings implicate resolution of taxane-related toxicities in long term survivors. Notably, patients in our analysis may have received taxanes and other neuropathy-associated regimens prior to receiving protocol-based HDCT – these agents were not consistently captured.

Our cohort admittedly lacks sufficient size to make substantial inferences regarding CM in related to HDCT. At a glance, the incidence of diabetes in our cohort (22%) does exceed recent estimates in a general population of patients between the ages of 45-64 (13.7%).(19) However, the incidence of antihypertensive use in our study (22%) is lower than recent estimates of use in a general population between 18-39 (26.8%), 40-49 (49.3%), and 50-59 (60.9%).(20) Clearly, larger efforts will be needed to characterize the true burden of CM in association with HDCT.

In the absence of data from comparative trials, HDCT and conventional dose chemotherapy both remain reasonable options for relapsed and refractory GCTs. Our dataset suggests that prolonged survival can be achieved with the TECTIC regimen followed by HDCT and ASCT. While multiple previous studies have characterized QOL in a heterogeneous population of long-term survivors, the current study specifically suggests reasonable maintenance of QOL parameters in patients who have received a standardized HDCT regimen.(21-24) These data can inform the risk-benefit discussion between clinicians and patients with relapsed or refractory GCTs considering the TECTIC regimen. Furthermore, they underscore the need to incorporate assessments of QOL in forthcoming studies assessing strategies for relapsed or refractory germ cell tumors. An ideal setting in which to implement this approach is in the aforementioned planned phase III study comparing HDCT with TI-CE to CDCT with TIP.(16) In addition to distinctions between clinical outcome, it would be imperative to understand the QOL and co-morbidities incurred amongst patients treated with these approaches.

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Figure 1.
PFS and OS for the overall cohort.

Table 1

Patient characteristics.

Demographics	
Male/female	47/1
Age at diagnosis: median (range)	27.7 (16.1-47.0)
Age at Treatment: median (range)	29.3 (16.6-49.4)
Histology	
Seminoma	4
Non-seminoma	44
Number of prior regimens	
1	3
2	39
3	6
Prognostic grouping by Beyer score	
Intermediate	34
Poor	14
Prognostic grouping by IGCCCG risk group	
Good	6
Intermediate	6
Poor	35
Unknown	1

Table 2

Grade 3/4 acute toxicities related to protocol-based therapy. One patient experienced grade 5 infection. (Cycle 1 = Palictaxel, etoposide and carboplatin; Cycle 2 = Paclitaxel, ifosfamide, and carboplatin).

	Grade 3	Grade 4	Grade 3	Grade 4
	N	N	N	N
Hyperglycemia	15	1	4	0
Transaminase alone	13	0	6	0
Mucositis/stomatitis	10	24	4	6
Nausea/vomiting	10	0	5	0
Neuropathy	10	0	0	0
Febrile neutropenia	4	0	1	0
Altered consciousness	4	0	0	0
Diarrhea	3	2	2	1
Hypotension	3	1	0	0
Hyperbilirubinemia	3	0	3	0
Elevated alkaline phosphatase	3	0	0	0
Hallucinations	3	0	0	0
Fever w/o neutropenia	2	1	2	0
Dermatitis	2	1	0	0
Hypomagnesemia	2	0	0	0
Pulmonary	2	0	0	0
Hypocalcemia	1	1	2	0
Hypertension	1	0	0	0
Colitis	1	0	0	0
Hematuria	1	0	0	0
GI Bleeding	1	0	0	0
Low Phosphate	1	0	0	0
Fluid Retention	1	0	0	0
Hemorrhage	1	0	0	1
Hypoxia	1	0	0	0
Hearing	1	0	0	0
Somnolence	1	0	0	0
Syncope	1	0	0	0
Myalgia	1	0	0	0
Infection (NOS)	1	0	0	0
Arrhythmia/infarction	0	3	0	0
Elevated INR/Prothrombin time	0	2	1	1
Renal Failure	0	1	0	1
Anorexia	0	1	0	0

	Grade 3	Grade 4	Grade 3	Grade 4
	N	N	N	N
Constipation	0	0	1	0
Esophagitis	0	1	1	0

Table 3

HR-QOL as assessed by the QLQ-C30 questionnaire. Results are compared to a cohort of patients assessed by the same survey by Rossen *et al.*(11)

Global Health Scale	87.04	14.64	75.62	20.30	0.02
Physical functioning	68.89	3.96	92.66	14.76	0.0001
Role functioning	97.22	8.57	90.83	20.08	0.18
Emotional functioning	88.89	17.85	85.01	19.45	0.42
Cognitive functioning	87.96	13.77	84.45	21.19	0.49
Social functioning	89.81	18.20	92.04	18.21	0.62
Fatigue	14.20	16.08	19.54	21.41	0.31
Nausea and vomiting	1.85	5.39	3.36	10.06	0.53
Pain	9.26	13.06	14.65	22.92	0.33
Dyspnea	11.11	16.17	8.50	16.96	0.54
Insomnia	12.96	20.26	17.45	24.99	0.46
Appetite loss	3.70	10.78	4.92	14.17	0.73
Constipation	1.85	7.86	3.58	12.93	0.58
Diarrhea	1.85	7.86	11.19	21.79	0.07
Financial difficulties	16.67	30.78	7.61	19.80	0.09

Table 4

Comparison of FACT-Taxane scores yielded from the current study (n=18) to those derived from a study by Cella *et al* assessing patients with NSCLC receiving conventional doses of taxane therapy (n=143) at baseline, 6-weeks and 12-weeks of treatment.

Current study	56.60	13.24	*
NSCLC patients (Baseline)	56.60	9.20	0.16
NSCLC patients (6-weeks)	53.20	9.10	0.93
NSCLC patients (12-weeks)	48.30	10.60	0.05

* Referent value.