

High-Dose Ifosfamide in Relapsed Advanced Synovial Sarcoma: A Phase II Study of Efficacy and Health-Related Quality of Life outcomes from India

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Abstract

Treatment options for advanced synovial sarcoma that has progressed beyond first-line therapy are severely scarce. This prospective, single-center, phase II Simon clinical trial evaluated high-dose ifosfamide 11 g/m² administered over 4 days every 21 days with mesna, prophylactic growth factors, and albumin supplementation for up to 6 cycles to determine an optimal regimen balancing efficacy, toxicity, and quality of life (QoL). Eligible participants were aged ≥ 16 years with metastatic or unresectable synovial sarcoma, measurable disease per RECIST v1.1, ECOG performance status 0–2, and progression after at least one prior line of therapy. Prior ifosfamide exposure was permitted.

Among 26 enrolled (median age: 30), 22 were evaluable for response. 35% had ECOG performance status 2. The ORR was 63.6%. Median PFS was 7.5 months (95% CI, 5.9–9.4), and median OS was not reached at median follow-up of 12 months. Greater number of prior treatment lines was independently associated with inferior PFS (hazard ratio, 4.83; 95% CI, 1.40–16.64). Grade 3 or higher treatment-related adverse events occurred in 77% of patients. Treatment discontinuation due to toxicity occurred in 15% of the patients. QoL analysis demonstrated significant declines in global health status and functional domains, despite improvements in pain and dyspnea.

High-dose ifosfamide at 11 g/m² demonstrated substantial efficacy with durable disease control in advanced synovial sarcoma. While treatment was associated with significant toxicity and QoL deterioration, symptomatic improvement supports its continued role as a key therapeutic option, particularly in the regions where access to cellular therapies is limited.

Novelty and impact

This phase II research confirms high-dose ifosfamide 11 g/m² as an effective salvage strategy for relapsed advanced synovial sarcoma, with a significant tumor response (63.6% ORR) and considerable disease control (7.5 months median PFS). Critically, it highlights key clinical trade-offs of dose escalation: while successfully palliating pain and dyspnea, treatment toxicity causes significant quality-of-life decrease, emphasizing the importance of careful patient selection and intensive supportive care.

1. Introduction

The current options in therapeutic landscape of advanced synovial sarcoma includes doxorubicin¹, high dose ifosfamide^{2,3}, gemcitabine-docetaxel⁴, pazopanib⁵, regorafenib⁶ and TCR gene modified T cell therapies⁷. High dose ifosfamide is defined as dose more than 10.5 gram/m² based on pharmacokinetic studies^{8,9}. Current evidence for high-dose ifosfamide in advanced synovial sarcoma bases itself mostly on two major studies. First prospectively done in 1994 (n = 13)² which showed response rate of 100% but the dose used in this study was 14–18 g/m². The other done retrospectively in 2012 by Rahal et al³ (n = 34) used a dose of 12 gram/m² which showed ORR of 44% and median PFS of 11.6 months. So far ideal dose of high dose ifosfamide in synovial sarcoma remains elusive.

Recently afamitresgene autoleucel which is a TCR gene modified T cell therapy which targets MAGE-4 abundantly expressed on synovial sarcoma which showed an ORR of 37%⁷. However, the advent of TCR therapies has not benefitted everyone as HLA A02 is mostly found in Caucasians¹⁰.

Despite emerging immunotherapies, high-dose ifosfamide remains the cornerstone of synovial sarcoma management. While being effective, its impact on quality of life (QoL) outcomes remains a significant knowledge gap; to date, no study has analyzed the QoL associated with this regimen. Given the trade-off between high efficacy and potential cumulative toxicity, understanding the symptomatic burden is also essential. Thus, bridging this gap, our prospective study evaluates its efficacy and impact on quality of life, reaffirming its role as a reasonable option for the selected patients.

2. Methods

This was a phase II Simon 2 stage minimax¹¹ single arm clinical trial conducted at All Indian Institute of Medical Sciences (AIIMS) from January 2024 to January 2026. The study was commenced after the approval from the Institute ethics committee () and CTRI (CTRI/2024/03/063743). Written informed consent was taken from all participants before including them in the study. Study schema shown in supplementary Figure I.

The participants were aged 16 yrs or above with advanced (metastatic or unresectable) synovial sarcoma with measurable disease as per RECIST v1.1¹² who had progressed on at least one line of therapy. Prior exposure to Ifosfamide was considered as well. The diagnosis of synovial sarcoma was made using histology, immunohistochemistry and confirmed using break-apart fluorescent in situ hybridization or Fusion for the X;18 translocation. The major inclusion criteria included an Eastern Cooperative Oncology Group performance status of 0–2, normal hematologic parameters (absolute neutrophil count > 1,500/dL, platelets > 100,000/dL and hemoglobin > 8 g/dL), normal renal function (glomerular filtration rate > 30 mL/min/1.73 m²), and normal hepatic function (AST/ALT < 2.5 times upper limit of normal [ULN], serum bilirubin < 1.5 times ULN, and alkaline phosphatase < 2.5 times ULN). Main exclusion criteria included pregnancy, active infection, and poorly controlled hypertension.

Participants fulfilling the inclusion criteria were started on high dose ifosfamide at 11 gram/m² along with MESNA administered at the dose of 100% of ifosfamide. It was administered as bolus doses over 2 hours with total dose split in 4 days along with albumin 20% 100 ml after ifosfamide on all 4 days and additionally, they received growth factor support for 5 days starting from day 6 with cycle repeated at 21 days. 6 cycles were planned in total. Evaluation for toxicities was done after each cycle of chemotherapy and were documented as per CTCAE v5.0. The administration of next cycle was delayed till recovery in case of hematological toxicities and treatment was discontinued if patient had grade 3 or 4 encephalopathy, grade 3 or 4 renal dysfunction and grade 4 infection. Quality of life (QoL) assessment was done by the European Organization for Research and Treatment of Cancer (EORTC)—the Core Quality of life Questionnaire (QLQ C30)¹³.

The primary outcome of the study was objective response rate (CR + PR) after 4 cycles of high dose ifosfamide. Secondary outcomes included assessing progression free survival (PFS), Overall survival (OS), Quality of life (QoL) analyses and toxicity profiles. PFS was defined as the time from initiation of study drug till confirmed progression or death due to any cause. Survival analysis was determined using Kaplan- Meier plots. Statistical analysis was done using Stata Corp (2017) (Stata Statistical Software: release 15. College station, TX: Stata Corp LLC and R Studio (2025). Workflow of the study is shown in Figure I. Workflow in stage 1 and stage 2 is shown in supplementary Figure II and III respectively.

3. Results

A total of 26 participants were recruited between January 2024 and November 2025 with January 25th, 2026 as the data cutoff point. The median age of the participants was 30 years (range 19–50) with females comprising 58% of the total participants. 65% of the patients had ECOG PS 1. Break-apart/fusion FISH was done in all patients and was positive as per the inclusion criteria. The most common primary sites of disease were extremities (85%). Most of the patients were metastatic i.e. 92%, with lungs (73%) being the most common site of distant metastasis. The median number of lines of therapy was 1 (1–5) with 100%, 80% and 42% of the participants exposed to an anthracycline and ifosfamide and pazopanib respectively. In 21 patients with prior ifosfamide exposure, median dose received was 9g/m² with median number of cycles i.e. 5 (range 3–6) and two-third of them (14 patients) received the same in the metastatic setting. Baseline median albumin was 4.27 mg/dl. Baseline characteristics are summarized in Table 1. Baseline laboratory parameters are provided in supplementary table I.

Efficacy

In the first stage of the Simon two-stage design, 13 patients were enrolled. Three patients were non-evaluable for response due to early treatment discontinuation (unacceptable toxicity, n = 2) and disease related death prior to assessment (n = 1). Among the 10 evaluable patients, 7 achieved partial responses (PR; r₁ = 7), meeting the prespecified criteria to proceed to the second stage.

In the second stage, an additional 13 patients were recruited. Two patients discontinued treatment after one cycle due to toxicity and were excluded from the per-protocol response analysis. Among the 11 evaluable patients in this stage, the ORR was 63.6% (n = 7). The study met its primary endpoint. Among the total population (n = 26), response evaluation after 4 cycles was done in 21 patients, five patients were not evaluable (toxicity after 1 cycle, n = 4; death due to disease progression, n = 1). One patient had clinical progression and expired before radiological evaluation considering this patient as PD, thus overall response rate was 63.6% (14/22). All documented responses were partial responses (PR) per RECIST v1.1. Detailed response distributions after four cycles are illustrated in Figure II. Evaluable response in the cohort is also summarized in supplementary table II. One patient underwent curative resection after significant partial response to 4 cycles of ifosfamide as shown in supplementary figure VII.

At a median follow-up of 12 months, the median progression-free survival (PFS) was 7.5 months (95% CI: 5.9–9.4). The 6-month PFS rate was 62% (95% CI: 42%–83%). Median overall survival (OS) was not reached at the time of analysis, with eight recorded events. Kaplan-Meier estimates for PFS and OS are depicted in Figure III.

Progression-free survival did not differ significantly according to ECOG performance status or prior ifosfamide exposure (log-rank $p = 0.18$ and $p = 0.58$, respectively). On the other hand, PFS differed significantly by the use of prior lines of therapy (log-rank $\chi^2 = 7.38$; $p = 0.007$). In cox proportional hazards models, poorer performance status was associated with a numerically increased risk of disease progression, although not reaching statistical significance (hazard ratio, 2.22; 95% CI, 0.67–7.35; $p = 0.19$). Prior ifosfamide exposure was not associated with PFS (hazard ratio, 1.43; 95% CI, 0.40–5.11; $p = 0.58$). Conversely, a greater number of prior lines of therapy was independently associated with a higher risk of progression in cox proportional hazard analysis (hazard ratio, 4.83; 95% CI, 1.40–16.64; $p = 0.013$). Statistical analysis is summarized in supplementary table III and supplementary figure VI.

Post- protocol therapy

Following disease progression ($n = 17$) or treatment discontinuation due to toxicity ($n = 4$), patients were transitioned to subsequent systemic lines of therapy. Among those who progressed, the most common subsequent regimens included pazopanib ($n = 8$), gemcitabine-docetaxel ($n = 4$), regorafenib ($n = 3$), trabectedin and anlotinib ($n = 1$). The four patients who discontinued protocol therapy due to adverse events subsequently received pazopanib ($n = 2$) or regorafenib ($n = 2$) upon recovery. Details of post-protocol interventions are provided in supplementary table IV.

QoL analyses

Patient-reported outcomes were evaluated using the EORTC QLQ-C30 (v3.0) at baseline and following four treatment cycles. Raw scores were linearly transformed to a 0–100 scale per EORTC guidelines, where higher scores represent superior functional/global health status or increased symptom burden, respectively.

Changes in HRQoL were analysed via paired-sample comparisons. At baseline, the cohort exhibited moderate impairment across all five functional domains (physical, role, emotional, cognitive, and social) alongside a substantial baseline symptom burden. Paired HRQoL assessments were available for 18 patients (69% of the cohort); while the remaining patients were unable to complete follow-up QoL assessments. Global health status (mean change – 15.7) and quality of life declined significantly ($p < 0.05$) following four cycles of chemotherapy. Functional domain scores demonstrated a modest but consistent deterioration.

In contrast, disease-related symptoms showed selective improvement. Pain (mean change – 24.6) and dyspnea (mean change – 11.1) scores improved following treatment relative to baseline, whereas treatment-related symptoms, including fatigue, nausea/vomiting, insomnia, and appetite loss, worsened.

Constipation and diarrhoea scores remained largely unchanged, and financial difficulties persisted without significant improvement. Patient-reported quality-of-life outcomes, as measured by EORTC instruments, are summarized in Table 2 and presented visually in supplementary figure IV and V.

Toxicity profile

All patients experienced at least one treatment-related adverse event (TRAE). Grade 3 TRAEs occurred in 77% of the cohort (n = 20).

Neutropenia was the most prevalent toxicity, occurring in 77% of patients (grade 3/4: 54%). Febrile neutropenia was observed in four patients (15%; grade 3: n = 2; grade 4: n = 2). Anemia occurred in 42% of patients (grade 3: 23%), and thrombocytopenia in 23% (grade 3: 4%). The most common non-hematological toxicities were fatigue (23%) and nausea/vomiting (23%), all of which were grade 1 or 2. One patient (4%) developed renal dysfunction with proximal renal tubular acidosis and acute kidney injury after completing 6 cycles of ifosfamide.

Ifosfamide-related encephalopathy occurred in four patients (15%). Two patients experienced transient grade 1/2 confusion during cycle 1, which resolved and did not recur. Two patients developed grade 3 encephalopathy (hallucinations, disorientation, and sleep-cycle disturbances), necessitating permanent discontinuation. Both recovered with supportive care and later transitioned to trabectedin or regorafenib.

Permanent treatment discontinuation after one cycle occurred in four patients (15%) due to grade 4 febrile neutropenia (n = 2) and grade 3 encephalopathy (n = 2). Treatment delays due to toxicities were required for six patients (23%), primarily due to grade 4 neutropenia (n = 4) and grade 3 febrile neutropenia (n = 2). Adverse events are summarized in the supplementary table V.

4. Discussion

Our study is the first study to demonstrate efficacy of high dose ifosfamide (11 grams/m²) in advanced metastatic synovial sarcoma patients with an ORR of 63.6% and a median PFS of 7.5 months. We conducted this study with 11 g/m² as prior studies either used high doses which correlated to significant toxicities or was done retrospectively^{2,3}. Pharmacokinetic studies have shown that doses above 10.5 g/m² are considered as high dose ifosfamide as it follows saturation kinetics leading to receptor saturation and thus, increased toxicity. Any further increase in dose beyond 12 g/m² reports negligible increase in efficacy^{8,9}. So, we opted for 11 g/m² dose in order to reduce toxicity especially with inclusion criteria having both PS2 patients and patients with prior ifosfamide therapy.

The median age in our study i.e. 30 years is consistent with our previous clinical trials of gemcitabine-docetaxel⁴ and regorafenib⁶ in advanced synovial sarcoma, where median ages were 32 and 36 years, respectively. Whereas western cohort studies on advanced synovial sarcoma usually have a higher median age as seen in retrospective study of high dose ifosfamide³ (39 years) and in SPEARHEAD-1 trial

(41 years)⁷. Notably, 35% of the enrolled cohort presented with an ECOG performance status (PS) of 2 making this as only study of high dose ifosfamide with significant proportion of PS 2 patients. Most of the contemporary western trials in advanced synovial sarcoma including SPEARHEAD-1 trial with afamitresgene autoleucel had included only PS 0–1 patients with PS 2 patients excluded¹⁴. This moderate prevalence of PS 2 patients is consistent with our prior gemcitabine-docetaxel⁴ (41%) and regorafenib⁶ (46%) studies, reflecting the characteristically aggressive nature of advanced synovial sarcoma in real-world clinical settings. This cohort represents a high-risk, refractory population reflective of real-world practice, demonstrating the feasibility of the regimen despite extensive prior lines of therapy and poor performance status.

In advanced synovial sarcoma, gemcitabine-docetaxel produced an ORR of 4.5%⁴. Anti-angiogenic multikinase inhibitors also have less response rates, with pazopanib and regorafenib having an ORR of 6%⁵ and 12%⁶ respectively. Our primary objective, the ORR was 63.6% (PR in 14/22). The ORR exceeds the previous retrospective study of high dose ifosfamide in relapsed metastatic synovial sarcoma which was 44%³. This is in contrast to prior prospective study of high dose ifosfamide which showed 100% response rate presumably because all the patients in that study were ifosfamide naive and the dose used was significantly higher (14–18 g/m²). Compared to other chemotherapy options used in this setting, this regimen has highest ORR in relapsed setting. One patient in our study underwent curative surgical resection of metastasis after 6 cycles of high dose ifosfamide as she had significant radiological response.

At a median follow-up of 12 months, the observed responses were durable, with a median progression-free survival (mPFS) of 7.5 months, comparing these other options in this setting like gemcitabine-docetaxel, pazopanib, regorafenib with 3.0, 4.6, 5.8 months of median PFS respectively.^{4–6} Furthermore, the PFS is relatively less than the previously reported retrospective data for high-dose ifosfamide i.e. 11.6 months. However, this difference can be attributed to the retrospective nature of the previous study and possibly unstructured response evaluation. At the time of analysis, median overall survival (OS) was not reached while the estimated 12-month OS rate was 60%. Conspicuously, OS data were not reported in prior retrospective study evaluating ifosfamide at 12 g/m². These findings suggest that the current regimen provides a sustained clinical benefit in a population with limited therapeutic alternatives.

In Cox proportional hazards analysis, number of prior treatment lines were independently associated with inferior progression-free survival (PFS; $p < 0.05$). Patients who had received more than one prior line of therapy demonstrated inferior PFS relative to those treated after a single prior line. However, PFS was not associated with prior ifosfamide exposure. Collectively, these results support the earlier use of high-dose ifosfamide in patients with advanced or metastatic synovial sarcoma, particularly among individuals with preserved performance status and is willing for further chemotherapy even post standard dose of ifosfamide.

In this study, chemotherapy was associated with a complex pattern of health-related quality-of-life changes. Although disease-related symptoms such as pain and dyspnoea improved following treatment, this benefit did not translate into an overall improvement in patient-reported quality of life. Instead, global health status and functional domain scores declined, suggesting that treatment-related toxicity and cumulative burden outweighed symptomatic gains in many patients. The observed deterioration across physical, role, emotional, cognitive, and social functioning domains is consistent with the impact of multi-cycle systemic therapy on daily activities and psychosocial well-being highlighting the need for better supportive care measures. There was no difference in the financial burden scores as the drug is easily accessible and affordable. Taken together, these findings underscore the importance of balancing disease control with supportive care strategies aimed at mitigating treatment-related symptoms and preserving functional status during chemotherapy and similar to QoL changes with gemcitabine-docetaxel chemotherapy.⁴

As anticipated, most of the patients had hematological toxicity with grade 3/4 neutropenia being the most common despite all patients receiving prophylactic growth factor support. Other seen toxicities were febrile neutropenia, anemia and thrombocytopenia. This hematological toxicity profile was similar to the prior retrospective study of high dose ifosfamide at 12 g/m² which showed almost similar proportion of grade 3/4 neutropenia, febrile neutropenia and thrombocytopenia. Non-hematological side effects anticipated were encephalopathy which was countered by giving patients albumin infusion along with ifosfamide as patients with low albumin levels are at high risk of ifosfamide induced encephalopathy.¹⁵ However there is no strong evidence for albumin infusion to reduce the incidence of encephalopathy.¹⁶ In our study 2 patients who developed grade 1 encephalopathy were continued on ifosfamide while 2 different patients who had grade 2/3 encephalopathy were discontinued from study. Overall incidence of ifosfamide encephalopathy was higher compared to prior retrospective study of high dose ifosfamide which had 3% neurologic adverse event, presumably due to the increased proportion of PS 2 patients¹⁷ and reporting of graded adverse events due the prospective nature of this study. Also, the route of ifosfamide administration was bolus compared to previous studies which used continuous infusion method. However, there is no evidence for increased incidence of neurologic adverse events with bolus administration. One patient developed renal dysfunction with proximal RTA Fanconi syndrome and AKI, developing complication after completing 6 cycles of ifosfamide and eventually had a partial response to the treatment. Ifosfamide use is strongly associated with both Fanconi syndrome and type 1 tubular acidosis.¹⁸

In developed countries adoptive cellular therapies are used which utilizes engineered TCR cells against MAGE4 and NY-ESO1 which are abundantly expressed in synovial sarcoma¹⁹. Afamitresgene autoleucel⁷ is a FDA approved treatment option in advanced synovial sarcoma but the therapy is HLA A02 restricted which has a very low incidence in Asian population. There is delay in treatment involving T cell therapies as the median time from leukapheresis (collection of T-cells) to the release of the final manufactured product is 40 days as it is not an off-shelf treatment⁷. In SPEARHEAD-1 trial only 13% of all screened patients could receive therapy predominantly due to not fulfilling the criteria for required HLA and

sufficient MAGE-A4 expression.⁷ Hence, even in this era with T cell modified cellular therapies high dose ifosfamide remains a substantial treatment regime in the management of advanced synovial sarcoma and the feasible dose for maximizing efficacy and limiting side effects is 11 gram /m² as established by this study.

This is the only prospective study of high dose ifosfamide at 11 g/m² in advanced synovial sarcoma patients reporting significant response rate with durable PFS. This study included significant proportion of PS 2 patients as commonly seen in real world setting. To the best of our knowledge this is the only study of high dose ifosfamide with detailed QoL analysis.

This was a single center study and patients with prior ifosfamide exposure within one year were excluded hence, we don't know the effect of high dose ifosfamide in this population. As longer-term follow-up is done, updated survival results will be published. Extended follow-up will be essential to better define long-term survival and late toxicity profiles. Furthermore, translational initiatives that use predictive biomarkers and molecular profiling may improve patient selection, and guide individualized treatment plans.

Abbreviations

Abbreviations	Full term/Phrase
FISH	Fluorescence in Situ Hybridization
CR	Complete Response
PR	Partial Response
SD	Stable Disease
QoL	Quality Of Life
ECOG-PS	Eastern Cooperative Oncology Group (Performance Status)
RTA	Renal Tubular Acidosis
AKI	Acute Kidney Injury
HLA	Human Leukocyte Antigen
FDA	Food and Drug Administration
AIM	Adriamycin Ifosfamide Mesna
GD	Gemcitabine Docetaxel
IQR	Inter Quartile Range

Declarations

Funding- This study received no external funding.

Ethics approval and consent to participate- The study was conducted after approval from the Institute Ethics Committee of All India Institute of Medical Sciences, New Delhi (). The study was registered with the Clinical Trials Registry–India (CTRI/2024/03/063743). Written informed consent was obtained from all participants before enrolment

Competing interests- The authors declare that they have no competing interests.

Availability of data and materials - The datasets generated and analyzed during the current study are not publicly available due to patient privacy and clinical confidentiality, but are available from the corresponding author upon reasonable request.

Author Contribution

V.K. P R , recruited patients, acquired clinical data, participated in patient management, interpreted the data, and drafted the manuscript.S.R. conceptualized and designed the study, supervised the project, interpreted the data, critically revised the manuscript for important intellectual content, and approved the final version.A.S. contributed to data curation, statistical analyses, interpretation of results, preparation of tables and figures, and manuscript revision.K.S. contributed to data curation, statistical analysis, interpretation of the findings, revision of the manuscript.C.N. participated in patient recruitment, patient management, and manuscript review.L.K. coordinated and analysed the quality-of-life assessments, patient-reported outcomes, and reviewed the manuscript.S.A.S. contributed to imaging interpretation and response assessment and reviewed the manuscript.A.B. performed pathological evaluation, confirmed the diagnosis, interpreted pathological findings, and reviewed the manuscript.S.B. contributed to patient management, surgical evaluation, and manuscript review.A.J. contributed to patient management, and critical revision of the manuscript.S.S. contributed to radiological evaluation, imaging interpretation, response assessment, and manuscript review.S. G. supervised radiological assessment, interpreted imaging findings, and critically revised the manuscript.All authors read and approved the final manuscript.

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Tables

Table I: Baseline characteristics of the study population

Characteristic	Group	N (%)
Age, years	Median (IQR)	30 (19-50)
Age category	≤30 years	14 (53.8%)
	>30 years	12 (46.2%)
Sex	Male	11 (42.4%)
	Female	15 (57.6%)
ECOG PS	0-1	17 (65.4%)
	2	9 (34.6%)
Sites of disease	Extremities	22 (84.6%)
	Trunk	3 (11.6%)
	Visceral	1 (3.8%)
Disease status	Metastatic	24(92.3%)
	Unresectable	2(7.6%)
Prior Ifosfamide exposure (Median dose of 9 g/m2)	Yes	21(80.7%)
	No	5(19.3%)
Prior Surgery	Yes	15(57.6%)
	No	11(42.3%)

Prior Radiotherapy	Yes	11(42.4%)
	No	15(57.6%)
Sites of Metastasis		
	Lung	19 (73%)
	Bone	6(23%)
	Lymph node	4(15.3%)
	Pleural	4 (15.3%)
	Liver	3(11.5%)
	Pancreas	1(3.8%)
Number of previous lines of therapy	Median (range)	1 (1-5)
Prior Chemotherapy		
	Ifosfamide- Doxorubicin (AIM)	21(80.7%)
	Doxorubicin	5(19.3%)
	Gemcitabine- Docetaxel (GD)	1(3.8%)
	Gemcitabine-Dacarbazine	1(3.8%)
Prior Targeted therapy		
	Pazopanib	11(42.3%)

Table II: EORTC QLQ-C30 functional (higher scores indicate better functioning) and symptom scale (higher scores indicate greater symptom burden) scores at baseline and after four cycles of chemotherapy

Symptom Scale	n (paired)	Baseline mean ± SD	Post-4 cycles mean ± SD	Mean change	p value
Physical functioning	18	65.5 ± 20.0	49.4 ± 19.6	-16.1	<0.01
Role functioning	18	62.7 ± 16.2	49.0 ± 18.1	-13.7	<0.01
Emotional functioning	18	58.8 ± 13.7	41.7 ± 12.5	-17.2	<0.01
Cognitive functioning	18	56.9 ± 25.0	48.0 ± 24.9	-8.8	<0.01
Social functioning	18	55.9 ± 22.8	45.1 ± 20.2	-10.8	<0.01
Global health status / QoL	18	63.7 ± 19.8	48.0 ± 19.2	-15.7	<0.01
Functional Scale	n (paired)	Baseline mean ± SD	Post-4 cycles mean ± SD	Mean change	p value
Physical functioning	18	65.5 ± 20.0	49.4 ± 19.6	-16.1	<0.01
Role functioning	18	62.7 ± 16.2	49.0 ± 18.1	-13.7	<0.01
Emotional functioning	18	58.8 ± 13.7	41.7 ± 12.5	-17.2	<0.01
Cognitive functioning	18	56.9 ± 25.0	48.0 ± 24.9	-8.8	<0.01
Social functioning	18	55.9 ± 22.8	45.1 ± 20.2	-10.8	<0.01
Fatigue	18	38.4 ± 21.6	55.9 ± 22.4	+17.5	0.01
Nausea / vomiting	18	18.6 ± 17.9	41.2 ± 26.8	+22.6	0.01
Pain	18	58.7 ± 25.9	34.1 ± 24.3	-24.6	<0.01
Dyspnoea	18	27.4 ± 22.1	16.3 ± 18.7	-11.1	0.04
Insomnia	18	31.8 ± 26.4	39.6 ± 28.9	+7.8	0.18
Appetite loss	18	36.5 ± 27.3	49.8 ± 31.2	+13.3	0.03
Constipation	18	22.7 ± 24.6	25.1 ± 23.4	+2.4	0.72
Diarrhea	18	28.4 ± 26.1	29.1 ± 27.0	+0.7	0.88
Financial difficulties	18	66.4 ± 28.7	64.1 ± 30.2	-2.3	0.81

Supplementary Files

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