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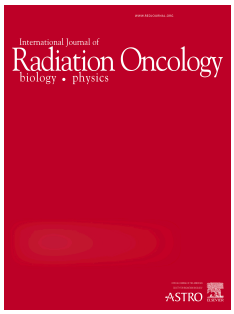

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Health related quality of life in SCALOP, a randomized phase II trial comparing chemoradiotherapy regimens in locally advanced pancreatic cancer (LAPC)

Short running title: SCALOP HRQL

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Conflict of interest:

Dr McDonald reports fees from Sanofi for advisory board participation outside the submitted work. Dr. Mukherjee reports grants, personal fees and non-financial support from Celgene, outside the submitted work.

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Health related quality of life in SCALOP, a randomized phase II trial comparing chemoradiotherapy regimens in locally advanced pancreatic cancer (LAPC)

Summary

SCALOP was a randomized, phase II trial in which patients with locally advanced, inoperable, pancreatic cancer were given capecitabine or gemcitabine based chemoradiation. This paper reports the health related quality of life (HRQL) data, including validation of the QLQ-PAN26 tool in CRT. The data support the use of chemoradiation as a treatment option (with capecitabine-based chemoradiation preferred) and the use of the QLQ-PAN26 as a valid tool.

Abstract

Purpose/Objective(s)

Chemoradiotherapy (CRT) for patients with LAPC provides survival benefits but may result in considerable toxicity. Health-related quality of life (HRQL) measures during CRT have not been widely reported. This paper reports HRQL data from the SCALOP trial, including validation of the QLQ-PAN26 tool in CRT.

Methods and Materials

Patients with locally advanced, inoperable, non-metastatic carcinoma of the pancreas were eligible. Following 12 weeks of induction gemcitabine plus capecitabine (GEMCAP) chemotherapy, patients with stable/responding disease were randomised to a further cycle of GEMCAP followed by capecitabine or gemcitabine based CRT. HRQL was assessed with the EORTC QLQ-C30 and PAN26.

Results

114 patients from 28 UK centres were registered and 74 patients randomized. There was improvement in the majority of the HRQL scales during induction chemotherapy. Significant deterioration in fatigue, appetite loss, and gastrointestinal symptoms during CRT recovered within 3 weeks following CRT. Differences in changes in HRQL scores between trial arms rarely reached statistical significance, however where they did, they favoured capecitabine. PAN26 scales had good internal consistency and were able to distinguish between subgroups of patients experiencing toxicity

Conclusions

Although there is deterioration in HRQL following CRT this resolves within 3 weeks. HRQL data support the use of capecitabine over gemcitabine-based chemoradiation. The QLQ-PAN26 is a reliable and valid tool to use in patients receiving CRT.

Introduction

Pancreatic cancer has a 5-year survival of less than 5% [1]. Treatment with chemoradiotherapy (CRT) may improve overall survival in patients with locally advanced inoperable tumours but may result in considerable toxicity.[2]. Health-related quality of life (HRQL) measures, not widely reported in the literature, are therefore relevant when interpreting trial data and in making treatment recommendations for patients with advanced pancreatic cancer.

SCALOP (Selective Chemoradiation in Advanced Localised Pancreatic Cancer) was a randomized phase II trial that compared gemcitabine based CRT (Gem-CRT) and capecitabine based CRT (Cap-CRT) following a course of induction chemotherapy in locally advanced pancreatic cancer (LAPC). SCALOP demonstrated that Gem-CRT was associated with more CTCAE grade 3/4 haematological and non-hematological toxicities and inferior median survival (13.4 vs 15.2 months, p=0.012) [3]. In SCALOP, HRQL was assessed with EORTC QLQ-C30 [4] and the pancreatic cancer module, the EORTC QLQ-PAN26 [5] which was developed for patients undergoing surgery, palliative chemotherapy and endoscopic treatment of pancreatic cancer; however it has not been previously validated in CRT.

This paper describes generic, disease- and treatment-specific HRQL during and after treatment with CRT. It also provides validation and reliability data on the QLQ-PAN26 in patients receiving CRT.

Methods and materials

Participants and methods

SCALOP was a multi-centre, open-label, randomised, parallel, two-arm, phase II trial conducted in the UK [3]. Patients with locally advanced, inoperable non-metastatic, histologically confirmed carcinoma of the pancreas were eligible. Registered patients received 3 cycles of gemcitabine and capecitabine (GemCap) chemotherapy and then restaged with CT scan of thorax, abdomen and pelvis. Patients with stable or responding disease (RECIST criteria, version 1.1), tumour diameter 6 cm or less and WHO performance status 0-1 were randomised 1:1 to either Gem-CRT or Cap-CRT by stratified minimisation with a random element (80:20). All participants provided written informed consent. The study was approved by the UK Medical Research and Ethics Committee (MREC) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). This study was registered at ISRCTN, number 96169987. The full protocol can be accessed at: http://www.wctu.org.uk/publications/scalop/SCALOP%20Clinical%20Protocol%20v4.0.pdf.

Treatment protocol

Induction chemotherapy consisted of 3 cycles of gemcitabine (1000mg/m^2 intravenously over 1 hr on days 1, 8 and 15 of a 28 day cycle) and capecitabine (830mg/m^2 orally, twice daily on days 1-21 of a 28 day cycle). Randomised patients received a further cycle of GemCap followed by concurrent chemoradiotherapy in combination with either gemcitabine (300mg/m^2 once per week) or capecitabine (830mg/m^2 twice daily on days of radiotherapy only). The total radiotherapy dose was

50.4Gy in 28 daily fractions over 5.5 weeks by use of 3D conformal or intensity modulated radiotherapy planning. No subsequent adjuvant therapy was given.

Health related quality of life

Health-related quality of life was assessed using the HRQL generic measure, the EORTC QLQ-C-30 [which assesses global quality of life, functional domains (physical, emotional, social, role and cognitive) and symptoms (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea, financial difficulty) that commonly occur in patients with cancer] [4] and a disease specific measure, the EORTC QLQ-PAN26 (pancreatic domain – which uses 26 questions hypothesised as 17 scales and single items specifically related to pancreatic disease symptoms, treatment side-effects and emotional issues) [5]. Patients self-completed paper questionnaires at 6 time points – week 0 (baseline), week 17 (post induction chemotherapy), week 23 (immediately post-CRT) and subsequently at follow-up (weeks 26, 39 and 52) even, where possible, if patients experienced disease progression. Questionnaires were included if completed within 1 week (4 weeks for week 39 and 52) of the specified time point. The EORTC standard scoring procedure is that function scales and items are defined such that higher scores represent better HRQL whilst symptom scales and items are defined such that higher scores indicate more symptoms (worse HRQL). The full list is reported in Table 1.

Data analysis

All randomised patients were included in the analysis. The analyses were pre-specified in the statistical analysis plan and performed on an intention to treat basis

[3]. All analyses were undertaken and graphs produced using STATA® statistical software version 13.0 (Stata Corp., College Station, Texas, USA).

Data were imputed according to EORTC guidance if less than half the items within a scale were missing [6]. Where data were missing from more than half the items within any scale, these scales were excluded from the analyses. When a complete questionnaire was missing, the reason for the missing questionnaire was ascertained and categorized.

We performed two sets of analyses, one looked at the change in HRQL during induction chemotherapy (week 0 to week 17) and the other looked at the change from start of CRT (week 17) and later time points to assess the specific impact of CRT on HRQL and difference between arms.

The changes in mean HRQL between earlier and later time-points in all patients was normally distributed (assessed using Shapiro–Wilk tests for normality) and were presented with mean scores at each time-point, changes in mean scores and 95% confidence intervals around those changes. Changes in scores of 10 or more points were considered clinically significant [7]. When this data was split by treatment arm to compare changes in HRQL during and after CRT, the data was no longer normally distributed and therefore Wilcoxon rank sum tests were used to compare changes between arms. We had no a priori hypotheses as to which specific scales would be most affected by which arm so we compared all scales and highlighted results at the $p<0.05$ level (and $p<0.01$ to reduce errors from multiple testing) in these exploratory analyses.

Psychometric testing of the QLQ-PAN26

Cronbach's alpha coefficient was calculated as a measure of reliability of the QLQ-PAN26 using data from the week 23 assessments. Cronbach's alpha measures inter-correlation between the test scores of related items within the scales and alpha value ≥ 0.70 indicates good consistency [8]. Construct validity was assessed by observed differences in the scales at the time point immediately after CRT (week 23) between the group of patients who had any CTCAE grade 3 or 4 adverse event recorded by nurses and those who did not. It was hypothesised that patients with grade 3 or 4 adverse events would report worse scores in more scales than patients without any events. Additional known group comparisons were made in the 'side effects scale' between patients with and without a Serious Adverse Reaction (SAR) persisting at the week 23 time point where symptoms are typically most severe. SARs were defined as serious adverse events with at least possible causal relationship to one of the trial medications (including radiotherapy).

Role of funding source

The study was funded by Cancer Research UK's Clinical trials Awards and Advisory Committee (CRUK 07/040) who had no role in study design, data collection, analysis or interpretation, or writing of this report.

Results

Between Dec 24, 2009 and Oct 25, 2011, 114 patients were registered into the trial from 28 hospitals across the UK. All patients were followed until progression, death or 12 month follow-up assessment. 74 patients were eligible for randomisation after 3

cycles of induction chemotherapy; 38 were allocated to receive Gem-CRT and 36 to receive Cap-CRT [3]. HRQL data from patients who failed to proceed to randomisation after induction are not included in this analysis because very few patients completed the questionnaire after disease progression.

Questionnaire compliance and missing data

Questionnaire compliance was good throughout the study, baseline data being available for 34 (94%) of 36 patients receiving Cap-CRT and 35 (92%) of 38 patients receiving Gem-CRT (Table 2a). Rates at the 39-week time point were reduced to 71% (Cap-CRT arm) and 66% (Gem-CRT arm). Importantly, fewer questionnaires were returned in the Gem-CRT arm during later time-points due to higher rates of progression and death. Details and reasons for missing questionnaires are shown in Table 2a. Table 2b suggests that those with missing questionnaires at later timepoints (particularly week 26 and 39) had worse overall survival than those who did complete questionnaires. No problems were reported regarding patients completing the questionnaires but Table 3 suggests that the scale on sexual satisfaction on the QLQ-PAN26 questionnaire was not completed as often as other scales. The reason for non-return was missing for more patients at week 23 compared to other weeks. The week 23 assessment involved a clinic visit that was not part of standard care and a number of centres did not return any CRFs for this timepoint so we cannot ascertain for certain the reason for non-completion although it is likely to be administration error.

We received 305 questionnaires from all patients across all timepoints. Only 8 of the 32 HRQL scales had at least one missing item in more than 3% of the 305 questionnaires. Of those 8 scales, 7 had at least one missing item in less than 7% of

the 305 questionnaires. The other scale, sexual dissatisfaction, had at least one missing item in 24% of the 305 questionnaires. Only those scales with more than at least half of the items completed could be imputed using the EORTC method – thus only one (sexual dissatisfaction) of the 32 scales had more than 3% of values imputed using the EORTC method.

Data from the 52 week follow up has been omitted from the further analyses due to the low return rate.

HRQL during induction chemotherapy (weeks 0-17)

Baseline scores for functional scales were all greater than 64, similar to findings in other studies of pancreatic cancer. The range of possible scores is 0-100; our unpublished data show median scores for function scales of 90-100 in patients with symptomatic gallstones and in a sample of normal individuals (C Johnson, unpublished data). Baseline scores for all symptom scores were below 50 except for future health concern (mean 58.18). For comparison, patients with symptomatic gallstones score their pain around 50, and normal individuals <5 (C Johnson, unpublished data).

Figure 2 and Table 3 show that, for all randomised patients, the mean changes in the majority of scales show improvement during induction chemotherapy with clinical significance achieved in the pain (-11.02; 95% CI: -18.08 to -3.96), appetite loss (-13.56; 95% CIs: -23.90 to -3.22), pancreatic pain (-14.32; 95% CI: -21.02 to -7.62), weight loss (-10.34; 95% CIs: -20.62 to -0.06), and future health (-10.30; 95% CIs: -

18.78 to -1.83) scales. QLQ-PAN26 questions relating to side effects from treatment indicated significant deterioration (14.97; 95% CIs: 5.38 to 24.55).

HRQL during and after CRT

Figure 3 and Table 4 show the mean changes in scale scores between week 17 (start of CRT) and later time-points of week 23 (at the end of CRT), week 26 (3 weeks post CRT), and week 39. Most scales deteriorated between the start (week 17) and end (week 23) of CRT. There was clinically significant deterioration in fatigue (11.70; 95% CIs: 5.34-18.07), appetite loss (19.57; 95% CIs: 7.65-31.48), and gastrointestinal symptoms (12.22; 95% CIs: 2.83-21.61) and no clinically significant improvements over this period. However, there were no significant differences in mean scores between week 17 and week 26, suggesting that recovery from the acute effects of CRT occurs within a 3-week period. At week 39 compared to week 17, there were clinically significant deteriorations in pain (10.96; 95% CIs: 0.52-21.41) and bloating (10.81; 95% CIs; 0.99-20.63).

HRQL by trial arm

Table 5 suggests that, due to chance, there were some imbalances in HRQL scale median scores at week 17 (the point of randomisation) between arms. Thus changes in score from week 17 and each subsequent time point were compared rather than absolute scores at each time point. Table 5 also shows the difference between trial arms in terms of change in scale scores between week 17 and later time points. The median change between week 17 and later time points was never worse in the Cap-CRT arm than in the Gem-CRT arm. The results of the Wilcoxon rank sum tests that compared the differences between changes in score suggest little difference

between arms but where differences were found, each favoured Cap-CRT. Between week 17 and 23 there were differences at the $p<0.05$ level between trial arms in the distribution of the change in the following scores: cognitive functioning (p=0.036), fatigue (p=0.046), bloating (p=0.035), and dry mouth (p=0.029). Between week 17 and 26, this was only significant for future health (p=0.033). Between week 17 and 39, this was significant for cognitive functioning (p=0.011), dry mouth (p=0.001), and body image (p=0.022). The only significant difference at the $p<0.01$ level was in dry mouth between week 17 and 39 (p=0.001). Graphs of these selected domains are shown in Figure 4.

Validation of the QLQ-PAN26 questionnaire during CRT

Cronbach's alpha was >0.7 for all scales (implying good internal consistency) except for the jaundice scale (r=0.46). The jaundice scale has the following two questions: "have you had itching?" and "to what extent was your skin yellow?" The correlation between the scores for these two questions was low (Pearson's correlation coefficient=0.37).

Table 6 shows the mean scores at week 23 in the group of patients who had any CTCAE grade 3 and 4 adverse events during CRT (primarily gastrointestinal and constitutional) and those who did not. Clinically significant differences were seen in 8 scales (primarily gastrointestinal and constitutional) with worse scores in the patients with more severe adverse events. There was a significantly worse mean score at 23 weeks in the "side effects of treatment" scale when comparing those who had a SAR during CRT and those who did not: 34.9 (n=44; 95% CIs: 27.0-

42.7) vs 50.0 (n=4; 95% CIs: -18.5-118.5) although the confidence intervals are wide due to the small numbers.

Discussion

In the SCALOP trial there was an improvement in the majority of the HRQL scales during induction chemotherapy. There was significant decline in a number of HRQL scales during CRT (fatigue, appetite loss, and gastrointestinal symptoms) but these recovered by 3 weeks after the end of CRT. We speculate that the clinically significant deteriorations in pain and bloating scores at week 39 is likely to have been due to disease progression, either clinical or sub-clinical – however, as only 6 patients with documented progression had HRQL recorded at week 39, this conclusion is conjectural. The exploratory comparisons of differences in HRQL scores between trial arms rarely reached statistical significance, however where they did, they all favoured Cap-CRT, providing support to our previously published data for the use of Cap-CRT rather than Gem-CRT.

How does SCALOP compare with other HRQL trials in LAPC? In the E4201 study which randomized patients to single agent gemcitabine and gemcitabine based CRT, decline in HRQL scores were noted during CRT, which returned to baseline levels within 9 weeks of completion of CRT [9]. Despite a large difference in Grade 4 toxicity between the arms, there were no statistically significant differences in median FACT-Hep scale score between the treatment arms. This may have been due to small patient numbers, or due to separation in time of the toxicity and the HRQL assessment, so that the toxicity had resolved when HRQL was

recorded. Short et al reported HRQL using QLQ C30 and QLQ PAN26 questionnaires from a single-arm study, which included LAPC (n=41) and post-operative patients (n=22) receiving induction gemcitabine followed by 5FU-based CRT [10]. CRT improved local symptoms (pain scores and digestive symptoms) and the authors suggested that patients with local symptoms at baseline are most likely to benefit from CRT. Serrano et al reported HRQL outcomes from a single arm phase II trial of 2 cycles neo-adjuvant gemcitabine-oxaliplatin based CRT (30Gy in 15 fractions concurrent with first cycle) in patients with borderline resectable and resectable tumours (n=71) [11]. This study reported a decline in global HRQL scores but an improvement in pancreatic pain at the end of neo-adjuvant treatment. Long-term outcome in the unresected population was not reported due to low rate of questionnaire return. Contrary to these studies, SCALOP showed a temporary deterioration in local symptoms following CRT, although improvements in local symptoms were seen during induction chemotherapy.

The comparison of HRQL outcomes between LAPC patients treated with chemotherapy alone versus CRT remains an important, but unanswered, question. The clinical outcome from the LAP 07 trial, randomizing patients between chemotherapy alone and chemotherapy followed by induction chemotherapy, has been reported in abstract form only [12]. This study showed no additional overall survival benefit for CRT over and above chemotherapy alone, calling into question the role of CRT in this disease. No HRQL data was collected in this trial.

This is the first study to validate the use of QLQ-PAN26 in patients receiving CRT, a treatment that was rarely used during its development. To our knowledge, the data presented here provide the most robust validation to date of the use of the QLQ-PAN26 in patients receiving CRT. Importantly, a range of scales and items showed deterioration between the start and end of CRT but with recovery by 3 weeks after the end of CRT. This corresponds well with expected side effects of CRT and demonstrates the ability of PAN26 to detect clinically relevant changes. The scales showed good correlation with nurse reported adverse events and treatment related toxicities. Finally, the scales also showed good internal consistency with the exception of the jaundice scale. This is not surprising, as all patients were free of jaundice during treatment.

Our study has several limitations. Patient numbers in each arm were relatively small resulting in wide confidence intervals and few of the observed differences achieve statistical significance. Also, when comparing arms, multiple tests were conducted which increased the probablity of obtaining a p value of less than 0.05 by chance. Additionally, HRQL data from registered patients who did not proceed to randomisation were not captured, restricting the longitudinal trends shown to a cohort of chemotherapy-selected patients with stable or responding disease and therefore better overall prognosis. Importantly, questionnaire return rates continued to decline through the study period and it is likely those patients who did not respond to questionnaires during follow up experienced a different HRQL profile. This may be a source of bias, however data attrition is a significant problem in all studies of pancreatic cancer, largely due to the nature of the disease and patients' frequent rapidly declining health. Our data collection rate compares favourably

with E4201 trial and Serrano et al where the HRQL questionnaire compliance was 40% at 9 months and 25% at 6 months respectively [11].

Despite these limitations, this study has confirmed the validity of the QLQ-PAN26 in patients receiving CRT. It provides detailed insight into HRQL following induction chemotherapy and consolidation CRT, which has not been previously described elsewhere. These data will be useful when discussing therapeutic options in patients with LAPC and lend further support to the use of capecitabine rather than gemcitabine as the concomitant cytotoxic in this setting. Importantly, our data help to dispel any previously held anxieties and beliefs that CRT is a toxic treatment that will inevitably detract from HRQL in patients with limited life expectancy. The role of CRT in this disease remains controversial and future trials in LAPC should incorporate HRQL end-points.

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Titles and footnotes for figures

Figure 1. Flow diagram

Figure 2. Changes in mean HRQL scores following induction chemotherapy (between week 0 and week 17) with 95% confidence intervals

NB Negative score indicates deterioration in both functional and symptom scales. Abbreviations as shown in Table 2.

Figure 3. Changes in mean HRQL scores following chemo RT (week 17 to later time points) with 95% confidence intervals

a. QLQ-C30
b. QLQ-PAN26

NB Negative score indicates deterioration in both functional and symptom scales. Abbreviations as shown in Table 2.

Figure 4. Changes in selected mean HRQL scores by treatment arm with 95% confidence intervals

a. Cognitive functioning (high score indicates better QoL)

b. Fatigue (low score indicates better QoL)

c. Bloating (low score indicates better QoL)

d. Dry mouth (low score indicates better QoL)

e. Body image (low score indicates better QoL)

f. Future health concerns (low score indicates better QoL)

Table 1. QLQ scales, abbreviations, and imputations

Scale	Abbreviation	QLQ	Items in scale	Number of questionnaires with at least one item of the scale missing*	Of those, number imputed by EORTC guidelines
Global	GQOL	C30	2	2	0
Functional					
Physical	Physical	C30	5	5	4
Role	Role	C30	2	2	0
Emotional	Emotional	C30	4	4	3
Cognitive	Cognitive	C30	2	0	0
Social	Social	C30	2	2	2
Symptoms					
Fatigue	Fatigue	C30	3	4	3
Nausea and vomiting	Nausea	C30	2	1	1
Pain	Pain	C30	2	5	5
Dyspnoea	Dyspnoea	C30	1	2	0
Insomnia	Insomnia	C30	1	2	0
Appetite loss	Appetite	C30	1	2	0
Constipation	Constipation	C30	1	1	0
Diarrhoea	Diarrhoea	C30	1	3	0
Financial difficulties	Financial	C30	1	2	0
Pancreatic pain	Panc Pain	PAN26	4	14	8
Bloating	Bloating	PAN26	1	8	0
Gastrointestinal	Gastro	PAN26	2	8	1
Taste loss	Taste	PAN26	1	7	0
Indigestion	Indigestion	PAN26	1	11	0
Flatulence	Flatulence	PAN26	1	8	0
Weight	Weight	PAN26	1	7	0
Weak limbs	Weak limbs	PAN26	1	7	0
Dry mouth	Dry mouth	PAN26	1	9	0
Jaundice	Jaundice	PAN26	2	15	8
Altered bowel habit	Bowel	PAN26	2	13	6
Poor body image	Image	PAN26	2	11	3
Side effects of treatment	Side effects	PAN26	1	21	0
Future health concern	Future	PAN26	1	9	0
Forward planning limited	Planning	PAN26	1	9	0
Satisfaction with healthcare	Healthcare	PAN26	2	16	9
Sexual dissatisfaction	Sexual	PAN26	2	72	14

*Of the total of 305 questionnaires received from all patients across all timepoints

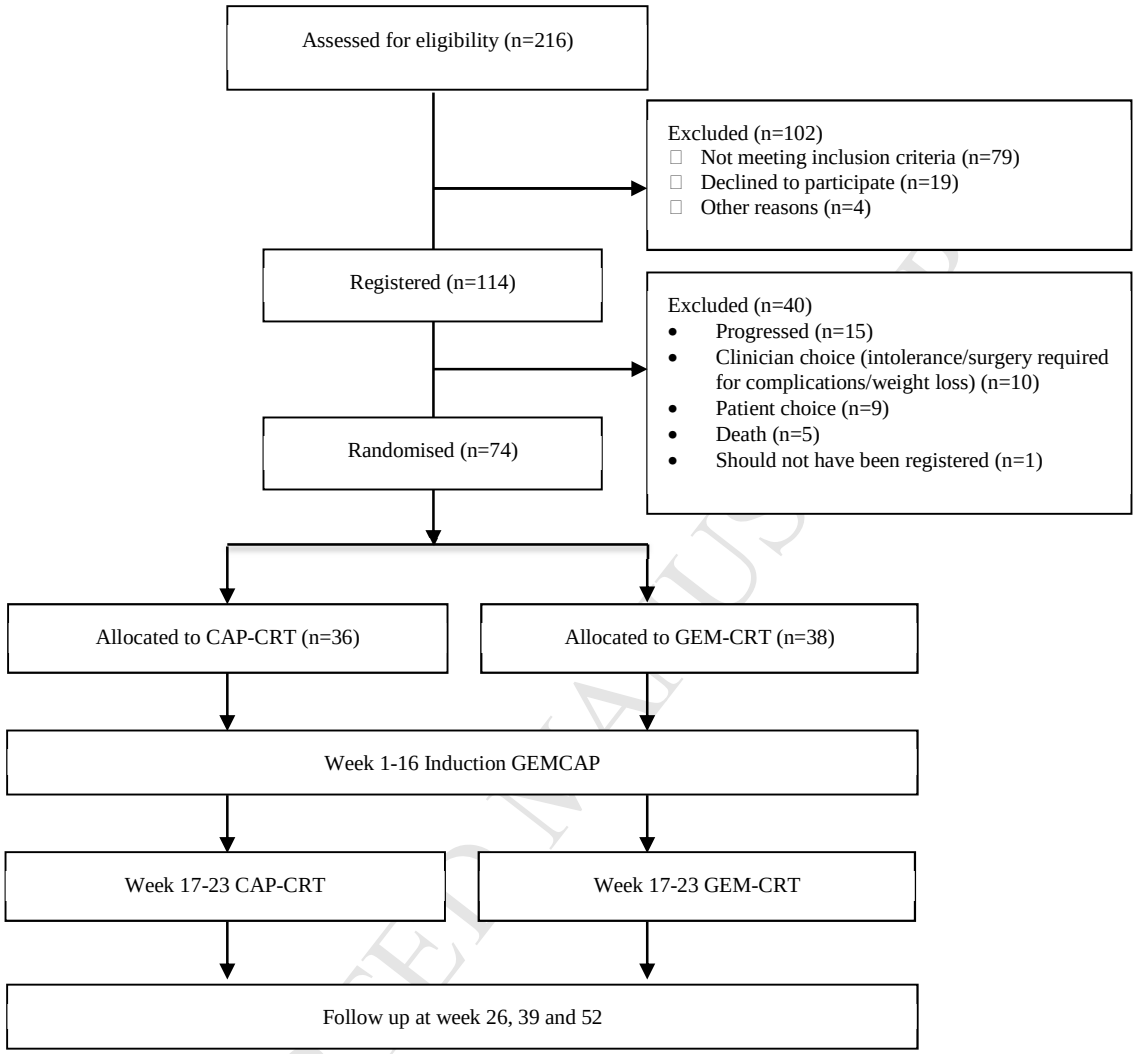
Table 2a. Questionnaire compliance and reasons for missing data by treatment group.

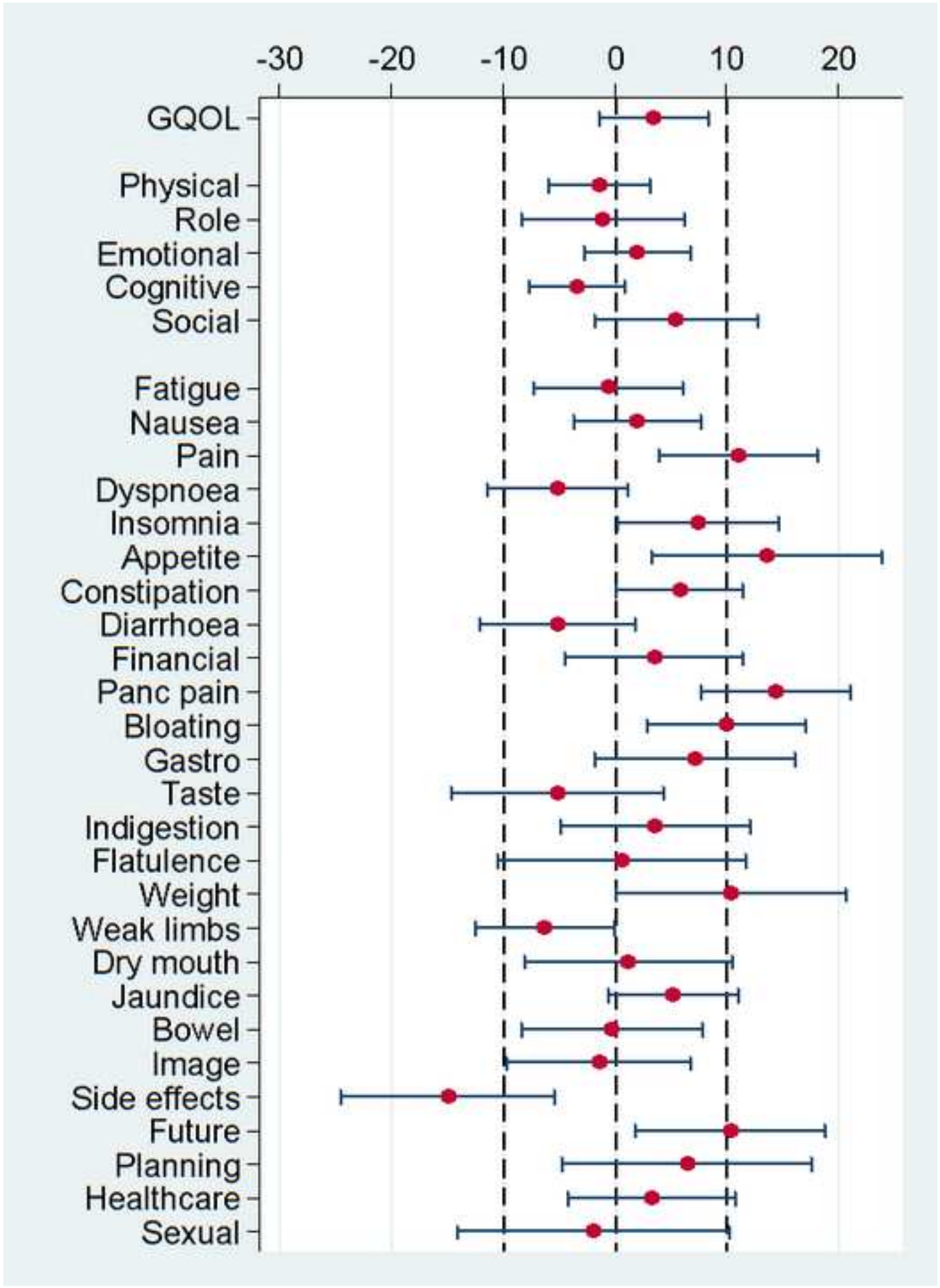
	RT + Capecitabine (n=36)												RT + Gemcitabine (n=38)											
	Baseline		17 week		23 week		26 week		39 week		52 week		Baseline		17 week		23 week		26 week		39 week		52 week	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patients still alive	36		36		35		35		34		29		38		38		37		36		29		24	
CRFs returned	34	94	31	86	23	66	24	69	24	71	19	66	35	92	30	79	26	70	27	75	19	66	13	54
Reasons for non-return																								
Admin error	1	3	3	8	3	9	6	17	2	6	3	10	3	8	3	8	3	8	3	8	2	7	1	4
Patient declined	0	0	0	0	0	0	0	0	1	3	0	0	0	0	1	3	1	3	0	0	2	7	0	0
Patient too unwell	0	0	2	6	1	3	4	11	4	12	7	24	0	0	0	0	1	3	2	6	4	14	8	33
Unknown	1	3	0	0	8	23	1	3	3	9	0	0	0	0	4	11	6	16	4	11	2	7	2	8

Table 2b. Overall survival at each timepoint by questionnaire completion

Timepoint	Patients with missing questionnaire		Patients with questionnaire	
	n	Overall survival (95% CIs)	n	Overall survival (95% CIs)
Week 17	13	14.6 (11.3-16.3)	61	15.8 (13.9-20.0)
Week 23	25	14.6 (10.3-16.3)	49	16.5 (14.0-21.5)
Week 26	23	12.7 (9.8-15.0)	51	19.1 (14.6-21.5)
Week 39	31	12.7 (9.5-14.0)	43	19.7 (15.7-23.1)

Figure 1. Flow diagram

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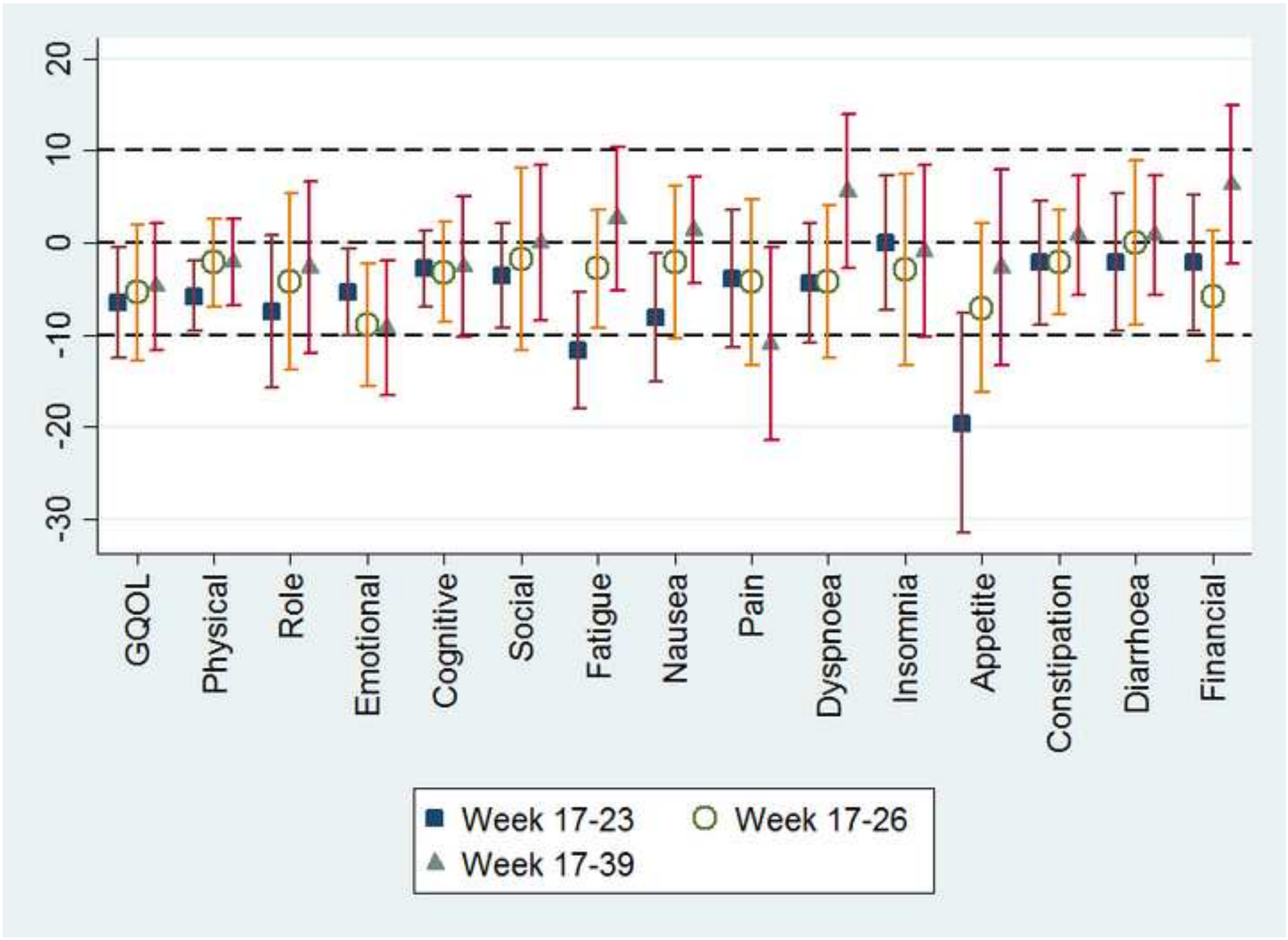
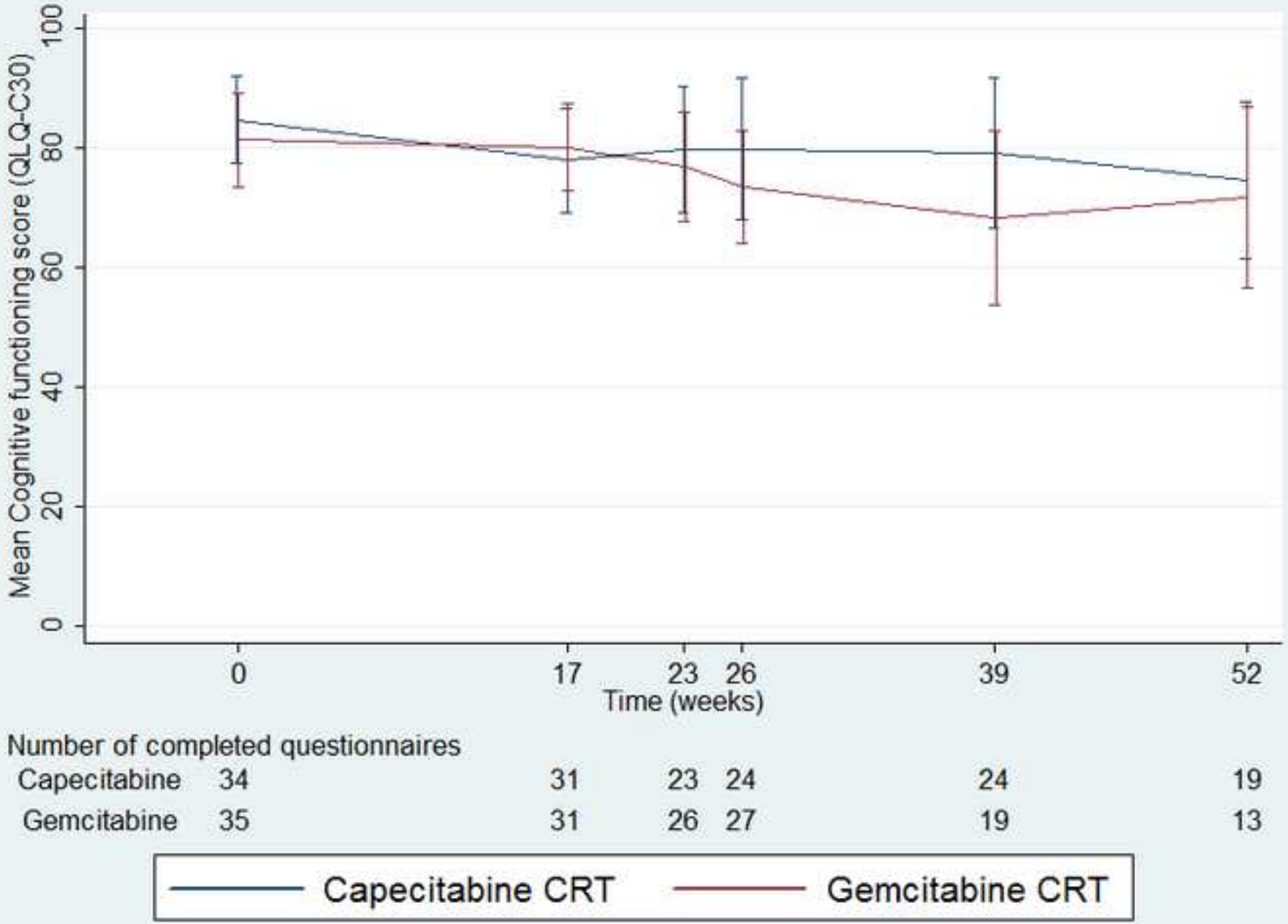
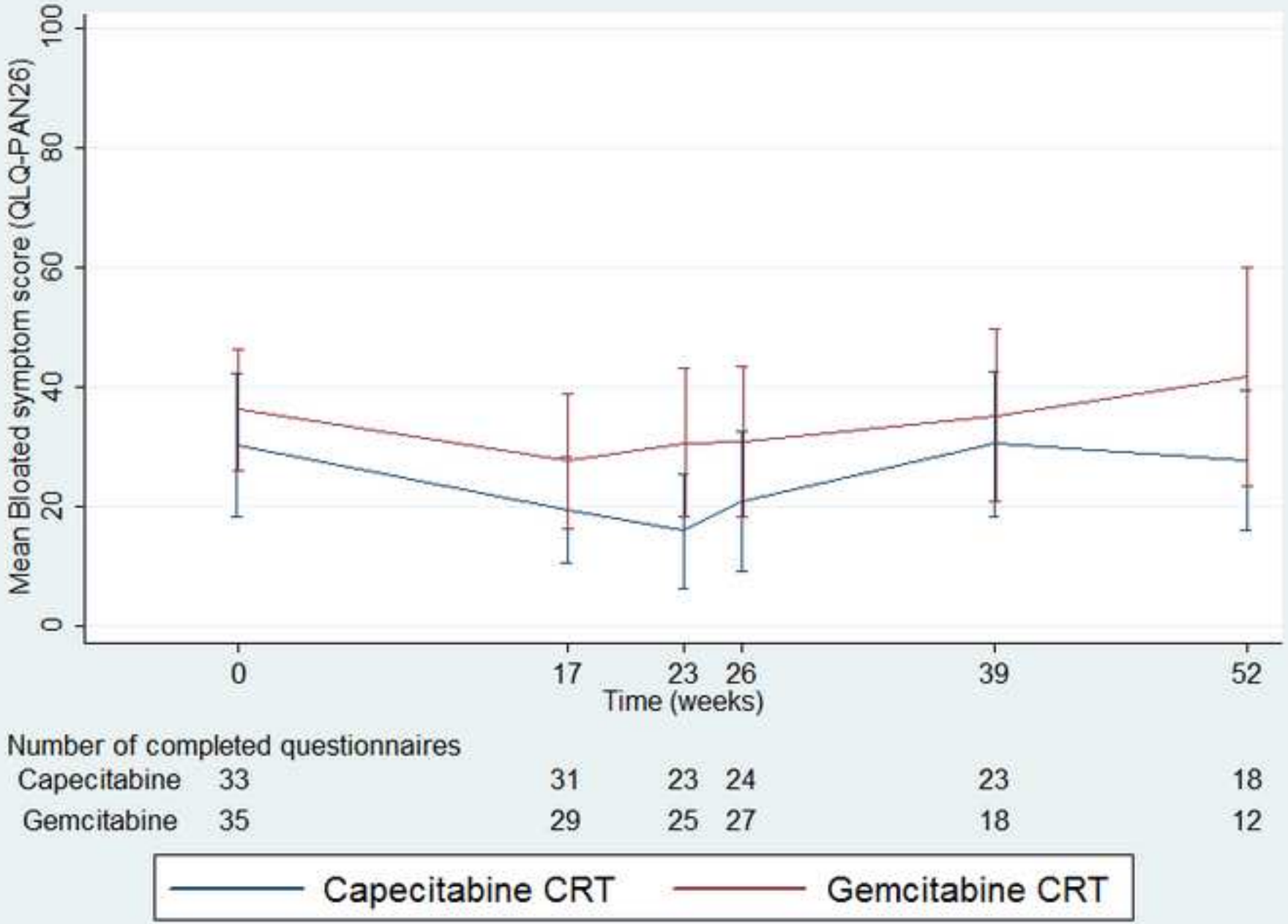
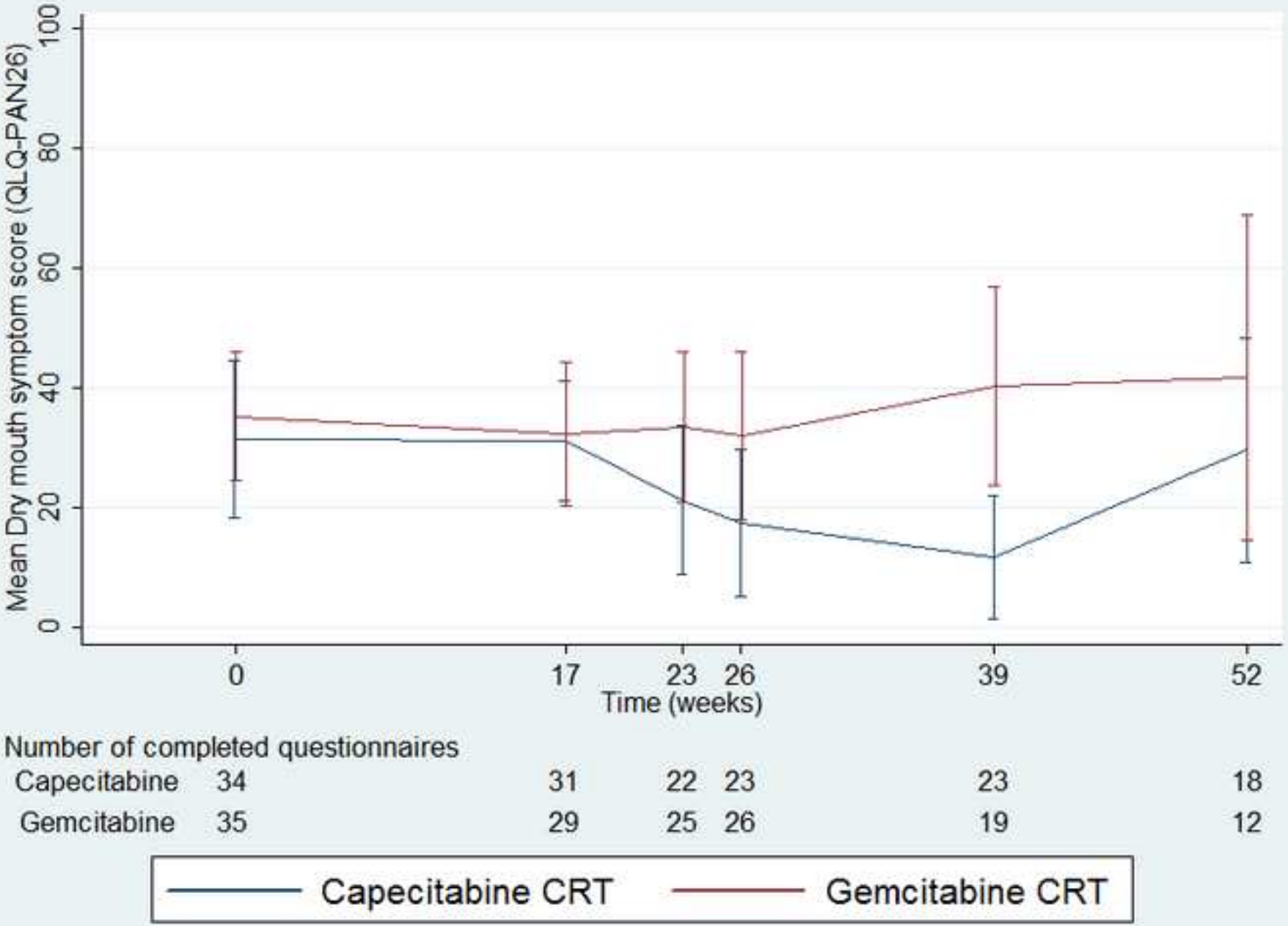
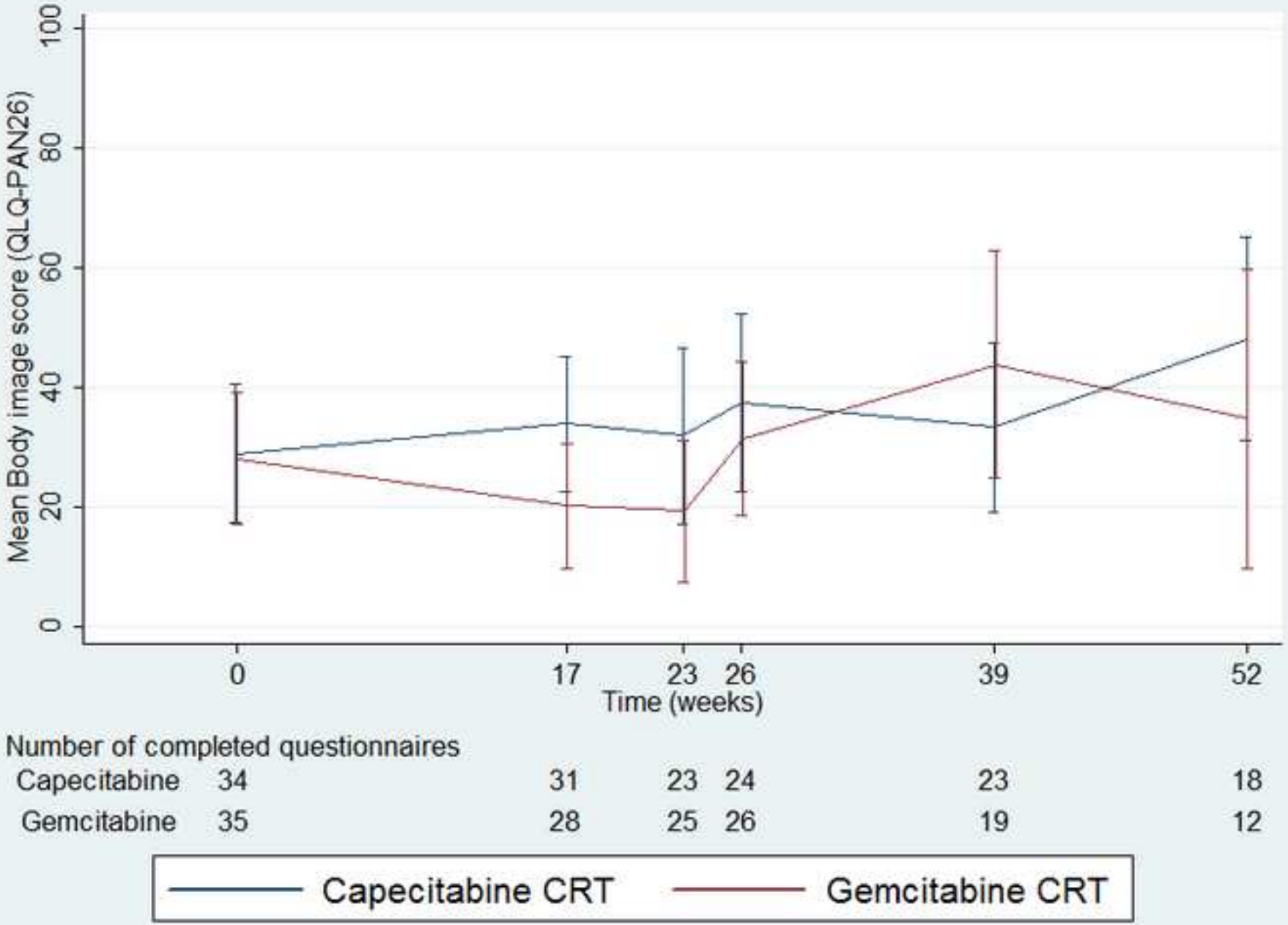
-20
-10
0
10
20
GQOL
Physical
Role
Emotional
Cognitive
Social
Fatigue
Nausea
Pain
Dyspnoea
Insomnia
Appetite
Constipation
Diarrhoea
Financial
Panc pain
Bloating
Gastro
Taste
Indigestion
Flatulence
Weight
Weak limbs
Dry mouth
Jaundice
Bowel
Image
Side effects
Future
Planning
Healthcare
Sexual

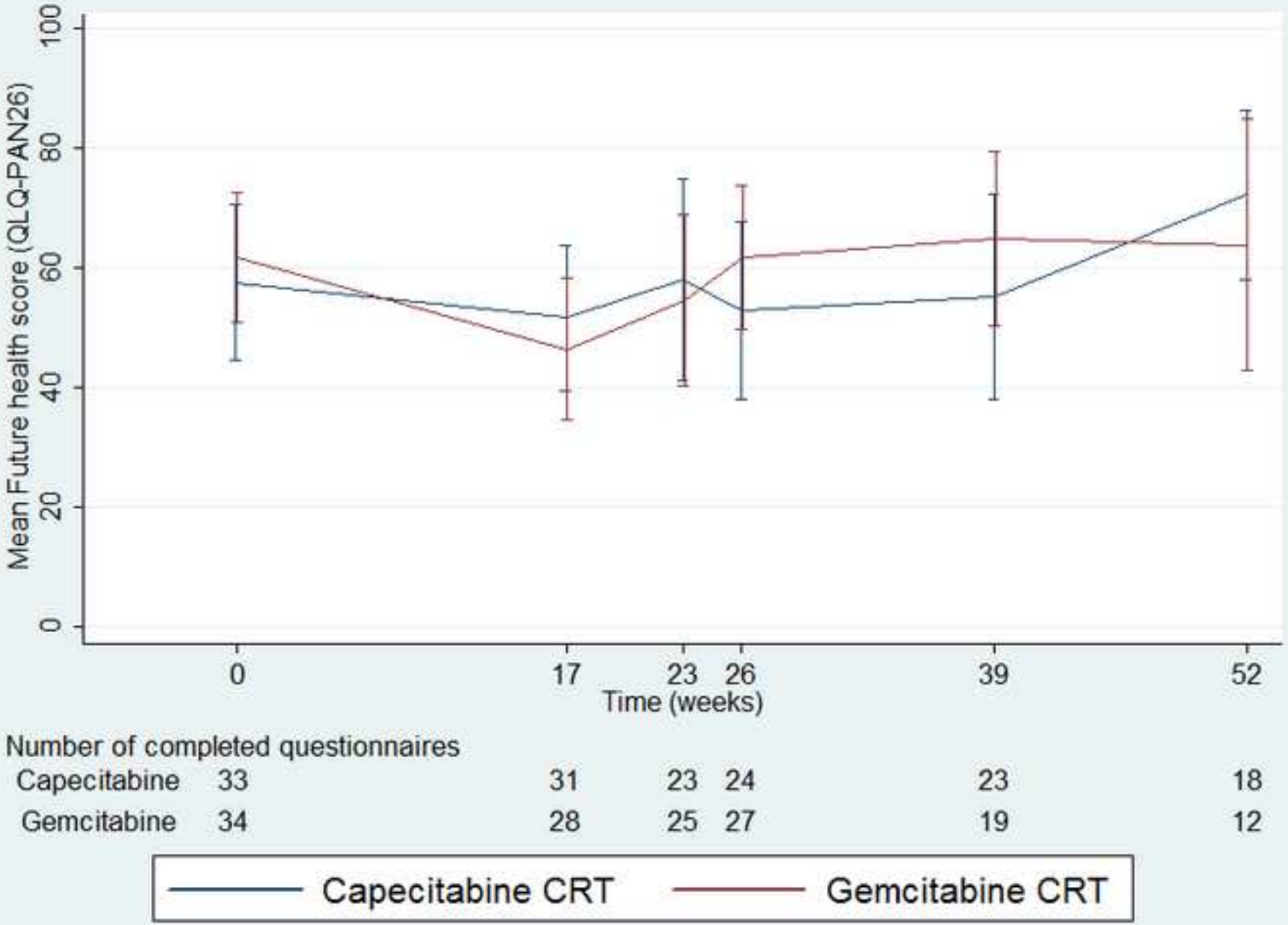

20
10
0
-10
-20
-30
GQOL
Physical
Role
Emotional
Cognitive
Social
Fatigue
Nausea
Pain
Dyspnoea
Insomnia
Appetite
Constipation
Diarrhoea
Financial
Week 17-23
Week 17-26
Week 17-39

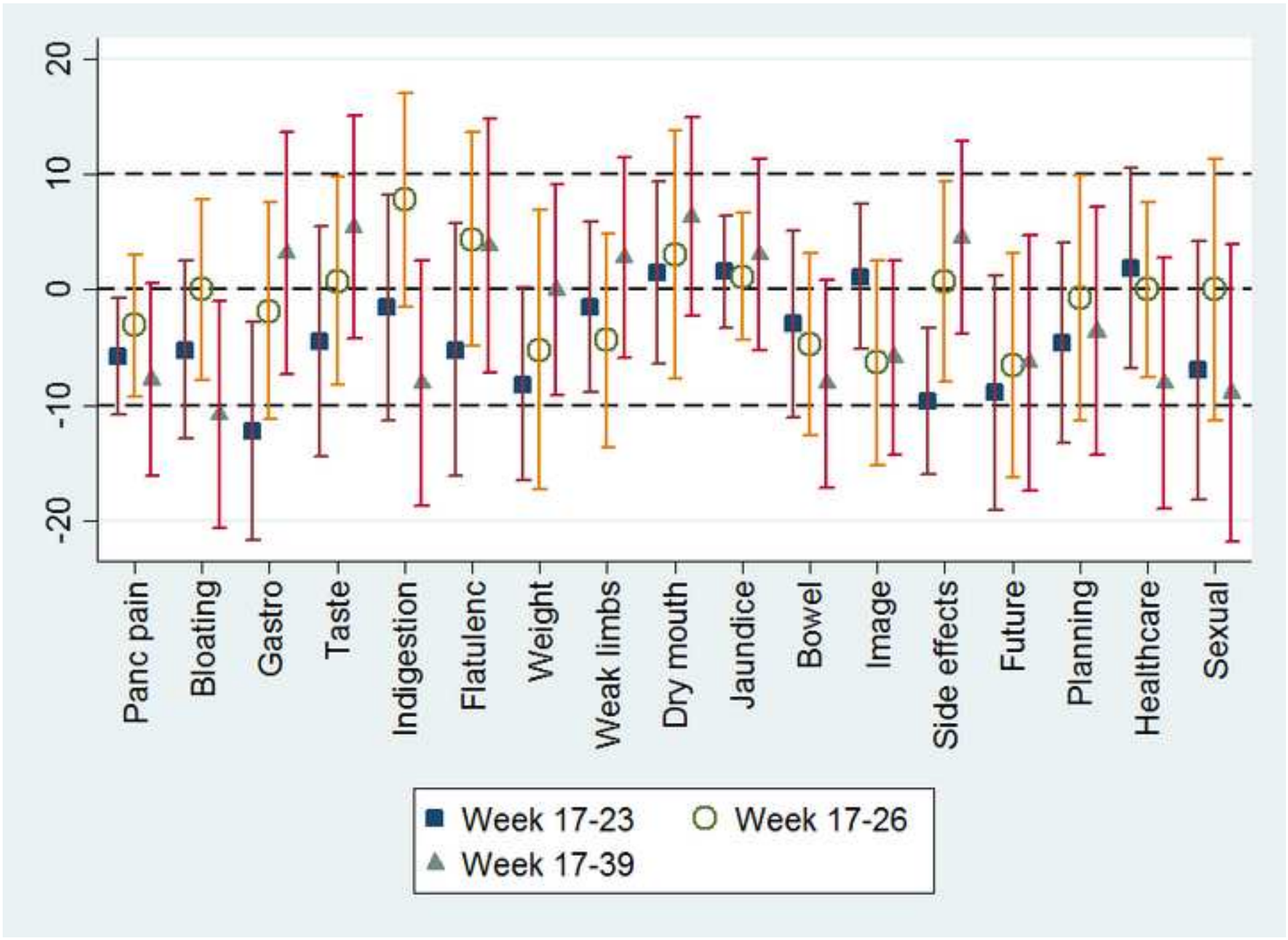

Mean Cognitive functioning score (QLQ-C30)
0
20
40
60
80
100
0
17
23
26
39
52
Time (weeks)
Number of completed questionnaires
Capecitabine 34 31 23 24 24 19
Gemcitabine 35 31 26 27 19 13
Capecitabine CRT
Gemcitabine CRT


Mean Bloated symptom score (QLQ-PAN26)
0
20
40
60
80
100
0
17
23
26
39
52
Time (weeks)
Number of completed questionnaires
Capecitabine 33 31 23 24 23 18
Gemcitabine 35 29 25 27 18 12
Capecitabine CRT
Gemcitabine CRT


Mean Dry mouth symptom score (QLQ-PAN26)
0
20
40
60
80
100
0
17
23
26
39
52
Time (weeks)
Number of completed questionnaires
Capecitabine 34 31 22 23 23 18
Gemcitabine 35 29 25 26 19 12
Capecitabine CRT
Gemcitabine CRT


Mean Body image score (QLQ-PAN26)
0
20
40
60
80
100
0
17
23
26
39
52
Time (weeks)
Number of completed questionnaires
Capecitabine 34 31 23 24 23 18
Gemcitabine 35 28 25 26 19 12
Capecitabine CRT
Gemcitabine CRT


Mean Future health score (QLQ-PAN26)
0
20
40
60
80
100
0
17
23
26
39
52
Time (weeks)
Number of completed questionnaires
Capecitabine 33 31 23 24 23 18
Gemcitabine 34 28 25 27 19 12
Capecitabine CRT
Gemcitabine CRT


20
10
0
-10
-20
Panc pain
Bloating
Gastro
Taste
Indigestion
Flatulenc
Weight
Weak limbs
Dry mouth
Jaundice
Bowel
Image
Side effects
Future
Planning
Healthcare
Sexual
Week 17-23
Week 17-26
Week 17-39

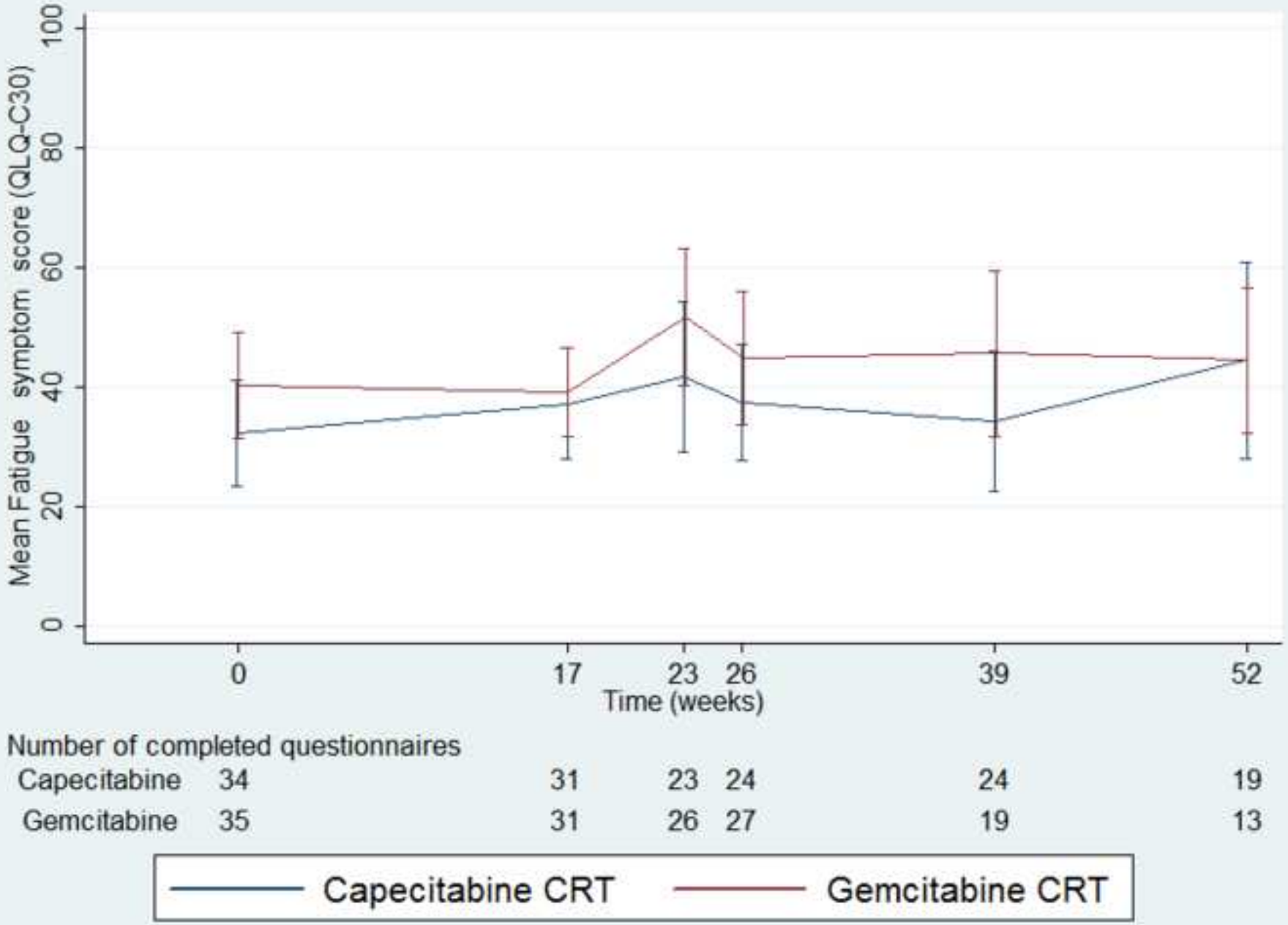

Mean Fatigue symptom score (QLQ-C30)
0
20
40
60
80
100
0
17
23
26
39
52
Time (weeks)
Number of completed questionnaires
Capecitabine 34 31 23 24 24 19
Gemcitabine 35 31 26 27 19 13
Capecitabine CRT
Gemcitabine CRT

Table 3. Mean difference in HRQL across all randomised patients between baseline and week 17 (induction chemotherapy)

Scale	n	Wk 0 µ	Wk 17 µ	Diff	lCI	uCI
Global	58	64.80	68.25	3.45	-1.46	8.36
Functional						
Physical	59	79.89	78.45	-1.44	-5.94	3.06
Role	59	70.90	69.77	-1.13	-8.43	6.17
Emotional	59	75.71	77.68	1.98	-2.77	6.72
Cognitive	59	82.20	78.81	-3.39	-7.64	0.86
Social	58	65.52	70.98	5.46	-1.85	12.77
Symptoms						
Fatigue	59	37.29	37.85	0.56	-6.12	7.25
Nausea	59	14.69	12.71	-1.98	-7.69	3.73
Pain	59	31.36	20.34	**-11.02**	-18.08	-3.96
Dyspnoea	58	13.22	18.39	5.17	-1.14	11.49
Insomnia	59	34.46	27.12	-7.34	-14.57	-0.12
Appetite	59	36.72	23.16	**-13.56**	-23.90	-3.22
Constipation	58	18.39	12.64	-5.75	-11.47	-0.03
Diarrhoea	58	20.11	25.29	5.17	-1.75	12.10
Financial	57	21.05	17.54	-3.51	-11.47	4.45
Panc Pain	58	36.83	22.51	**-14.32**	-21.02	-7.62
Bloating	57	32.75	22.81	-9.94	-17.03	-2.86
Gastro	58	35.92	28.74	-7.18	-16.14	1.78
Taste	58	27.01	32.18	5.17	-4.37	14.72
Indigestion	56	25.60	22.02	-3.57	-12.03	4.88
Flatulence	58	48.85	48.28	-0.57	-11.65	10.50
Weight	58	40.80	30.46	**-10.34**	-20.62	-0.06
Weak limbs	58	27.01	33.33	6.32	0.08	12.56
Dry mouth	58	32.18	31.03	-1.15	-10.43	8.13
Jaundice	55	16.97	11.82	-5.15	-10.96	0.66
Bowel	58	34.48	34.77	0.29	-7.78	8.35
Image	57	26.02	27.49	1.46	-6.78	9.70
Side effects	49	15.65	30.61	**14.97**	5.38	24.55
Future	55	58.18	47.88	**-10.30**	-18.78	-1.83
Planning	57	40.35	33.92	-6.43	-17.58	4.71
Healthcare	57	85.96	89.18	3.22	-4.28	10.71
Sexual	43	50.00	51.94	1.94	-10.23	14.11

Abbreviations: µ=mean; lCI=lower 95% confidence interval; uCI=upper 95% confidence interval; Diff= difference between means

NB High scores in function scales (and SatHC) represent better HRQLand higher scores in symptom scales represent worse HRQL. Negative differences in function scales represent HRQLworsening whereas negative differences in symptom scores represents HRQL improvement. Clinically significant differences are highlighted in bold.

Table 4. Mean difference in HRQL across all randomised patients between week 17 and later timepoints

	Week 23-17						Week 26-17						Week 39-17					
Scale	**n**	**Wk 17 µ**	**Wk 23 µ**	**Diff**	**lCI**	**uCI**	**n**	**Wk 17 µ**	**Wk 26 µ**	**Diff**	**lCI**	**uCI**	**n**	**Wk 17 µ**	**Wk 39 µ**	**Diff**	**lCI**	**uCI**
Functional																		
GQOL	46	68.84	62.32	-6.52	-12.49	-0.55	46	67.39	61.96	-5.43	-12.76	1.89	37	66.44	61.71	-4.73	-11.62	2.16
Physical	47	77.84	72.06	-5.78	-9.65	-1.91	47	78.55	76.35	-2.20	-6.95	2.55	37	76.76	74.59	-2.16	-6.88	2.55
Role	47	70.92	63.48	-7.45	-15.66	0.77	47	69.15	64.89	-4.26	-13.85	5.34	37	66.22	63.51	-2.70	-12.01	6.61
Emotional	47	78.55	73.17	-5.38	-10.08	-0.68	47	76.95	68.09	-8.87	-15.51	-2.22	38	77.85	68.64	-9.21	-16.49	-1.93
Cognitive	47	80.50	77.66	-2.84	-6.96	1.29	47	79.08	75.89	-3.19	-8.65	2.27	38	76.75	74.12	-2.63	-10.22	4.96
Social	46	69.20	65.58	-3.62	-9.33	2.08	46	66.67	64.86	-1.81	-11.72	8.10	37	63.06	63.06	0.00	-8.49	8.49
Symptoms																		
Fatigue	47	35.22	46.93	**11.70**	5.34	18.07	47	38.06	40.90	2.84	-3.53	9.20	38	40.35	37.72	-2.63	-10.39	5.12
Nausea	47	12.06	20.21	8.16	1.17	15.14	47	13.12	15.25	2.13	-6.07	10.33	38	11.84	10.53	-1.32	-7.07	4.43
Pain	47	20.92	24.82	3.90	-3.54	11.34	47	21.99	26.24	4.26	-4.73	13.24	38	20.61	31.58	**10.96**	0.52	21.41
Dyspnoea	46	19.57	23.91	4.35	-2.12	10.82	47	20.57	24.82	4.26	-4.06	12.57	36	22.22	16.67	-5.56	-13.87	2.75
Insomnia	47	26.24	26.24	0.00	-7.36	7.36	46	28.26	31.16	2.90	-7.50	13.30	37	27.93	28.83	0.90	-8.36	10.16
Appetite	46	19.57	39.13	**19.57**	7.65	31.48	47	23.40	30.50	7.09	-2.02	16.20	37	23.42	26.13	2.70	-7.90	13.30
Constipation	46	14.49	16.67	2.17	-4.56	8.90	46	15.94	18.12	2.17	-3.50	7.85	38	15.79	14.91	-0.88	-7.37	5.61
Diarrhoea	47	19.86	21.99	2.13	-5.34	9.60	46	23.19	23.19	0.00	-8.85	8.85	38	21.93	21.05	-0.88	-7.37	5.61
Financial	46	20.29	22.46	2.17	-5.18	9.52	46	18.12	23.91	5.80	-1.22	12.81	37	20.72	14.41	-6.31	-14.93	2.32
Panc Pain	45	21.85	27.59	5.74	0.72	10.77	46	24.46	27.54	3.08	-3.03	9.19	37	22.45	30.18	7.73	-0.55	16.02
Bloating	45	19.26	24.44	5.19	-2.50	12.87	46	25.36	25.36	0.00	-7.81	7.81	37	20.72	31.53	**10.81**	0.99	20.63
Gastro	45	25.56	37.78	**12.22**	2.83	21.61	46	30.80	32.61	1.81	-7.59	11.22	37	27.03	23.87	-3.15	-13.62	7.31
Taste	45	31.11	35.56	4.44	-5.48	14.37	46	36.96	36.23	-0.72	-9.70	8.25	37	29.73	24.32	-5.41	-15.04	4.22
Indigestion	44	20.45	21.97	1.52	-8.25	11.28	43	25.58	17.83	-7.75	-16.94	1.43	37	22.52	30.63	8.11	-2.50	18.72

Flatulence	45	43.70	48.89	5.19	-5.69	16.06	46	47.10	42.75	-4.35	-13.59	4.89	35	53.33	49.52	-3.81	-14.84	7.22
Weight	45	30.37	38.52	8.15	-0.16	16.46	45	29.63	34.81	5.19	-6.88	17.25	37	31.53	31.53	0.00	-9.07	9.07
Weak limbs	45	30.37	31.85	1.48	-5.90	8.86	46	31.16	35.51	4.35	-4.89	13.59	36	33.33	30.56	-2.78	-11.46	5.91
Dry mouth	44	28.79	27.27	-1.52	-9.38	6.35	44	29.55	26.52	-3.03	-13.70	7.64	37	28.83	22.52	-6.31	-14.93	2.32
Jaundice	43	10.08	8.53	-1.55	-6.41	3.30	44	10.23	9.09	-1.14	-6.64	4.37	33	13.64	10.61	-3.03	-11.32	5.26
Bowel	45	31.11	34.07	2.96	-5.12	11.04	46	35.51	40.22	4.71	-3.21	12.63	37	37.39	45.50	8.11	-0.84	17.05
Image	45	25.93	24.81	-1.11	-7.37	5.15	45	27.78	34.07	6.30	-2.53	15.12	37	28.83	34.68	5.86	-2.55	14.26
Side effects	45	28.15	37.78	9.63	3.36	15.90	45	34.07	33.33	-0.74	-9.41	7.93	37	35.14	30.63	-4.50	-12.86	3.85
Future	45	48.89	57.78	8.89	-1.22	18.99	46	51.45	57.97	6.52	-3.18	16.22	37	50.45	56.76	6.31	-4.76	17.37
Planning	44	34.09	38.64	4.55	-4.08	13.18	46	37.68	38.41	0.72	-9.81	11.26	37	38.74	42.34	3.60	-7.13	14.34
Healthcare	45	89.63	91.48	1.85	-6.77	10.47	46	92.03	92.03	0.00	-7.60	7.60	37	92.34	84.23	-8.11	-18.96	2.74
Sexual	36	53.70	60.65	6.94	-4.20	18.09	38	53.95	53.95	0.00	-11.32	11.32	30	49.44	58.33	8.89	-3.95	21.73

Abbreviations: μ=mean; lCI=lower 95% confidence interval; uCI=upper 95% confidence interval; Diff= difference between means; scale abbreviations as shown in Table 1.
NB High scores in functioning scales (and SatHC) represent better HRQL and higher scores in symptom scales represent worse HRQL. Negative differences in functioning scales (and SatHC) represent HRQLworsening whereas negative differences in symptom scores represent HRQLimprovement. Clinically significant differences are highlighted in bold.

Table 5. Difference in HRQL between week 17 and later timepoints by trial arm

	Week 23-Week 17								Week 26-Week 17						Week 39-Week 17					
	Capecitabine			Gemcitabine					Capecitabine		Gemcitabine				Capecitabine		Gemcitabine			
Scale	Median score week 17	n	Median difference in score (range)	Median score week 17	n	Median difference in score (range)	z	p	n	Median difference in score (range)	n	Median difference in score (range)	z	p	n	Median difference in score (range)	n	Median difference in score (range)	z	p
Func.																				
GQOL	66.7	23	0.0 (-33.3,41.7)	66.7	23	-16.7 (50.0,33.3)	1.70	0.090	23	0.0 (-50.0,50.0)	23	0.0 (-83.3,33.3)	0.57	0.571	23	0.0 (-41.7,33.3)	14	-8.3 (-58.3,33.3)	1.21	0.227
Physical	86.7	23	0.0 (-40.0,26.7)	73.3	24	-10.0 (-33.3,20.0)	1.58	0.114	23	0.0 (-33.3,26.7)	24	0.0 (-66.7,26.7)	-0.24	0.808	22	0.0 (-13.3,26.7)	15	-6.7 (-40.0,13.3)	1.28	0.199
Role	83.3	23	0.0 (-50.0,66.7)	66.7	24	-16.7 (-66.7,66.7)	1.11	0.268	23	0.0 (-50.0,66.7)	24	-16.7 (-100.0,66.7)	1.13	0.259	22	0.0 (-50.0,50.0)	15	0.0 (-66.7,33.3)	1.22	0.223
Emotional	83.3	23	0.0 (-58.3,16.7)	75.0	24	0.0 (-58.3,25.0)	-0.17	0.869	23	0.0 (-33.3,25.0)	24	-8.3 (-83.3,41.7)	1.67	0.094	23	-8.3 (-50.0,16.7)	15	-8.3 (-75.0,50.0)	0.53	0.598
Cognitive	83.3	23	0.0 (-16.7,16.7)	83.3	24	0.0 (-33.3,33.3)	2.10	**0.036**	23	0.0 (-33.3,33.3)	24	0.0 (-66.7,16.7)	1.19	0.233	23	0.0 (-66.7,33.3)	15	-16.7 (-50.0,33.3)	2.54	**0.011**
Social	83.3	23	0.0 (-66.7,50.0)	66.7	23	0.0 (-33.3,33.3)	0.19	0.848	23	0.0 (-66.7,66.7)	23	0.0 (-100.0,33.3)	0.80	0.422	23	0.0 (-66.7,50.0)	14	0.0 (-66.7,33.3)	-0.02	0.987
Symp.																				
Fatigue	33.3	23	11.1 (-33.3,44.4)	33.3	24	16.7 (-33.3,55.6)	-1.99	**0.046**	23	0.0 (-44.4,33.3)	24	0.0 (-33.3,77.8)	-0.45	0.652	23	-11.1 (-66.7,33.3)	15	-11.1 (-22.2,44.4)	-1.47	0.142
Nausea	0.0	23	0.0 (-33.3,50.0)	16.7	24	8.3 (-50.0,83.3)	-1.00	0.320	23	0.0 (-33.3,50.0)	24	0.0 (-66.7,100.0)	0.38	0.700	23	0.0 (-33.3,50.0)	15	0.0 (-33.3,0.0)	1.83	0.067
Pain	16.7	23	0.0 (-33.3,33.3)	16.7	24	0.0 (-66.7,83.3)	-1.36	0.174	23	0.0 (-50.0,66.7)	24	0.0 (-66.7,100.0)	-0.79	0.431	23	0.0 (-66.7,66.7)	15	16.7 (-50.0,66.7)	-0.61	0.545
Dyspnoea	0.0	22	0.0 (-66.7,33.3)	33.3	24	0.0 (-33.3,66.7)	-1.52	0.129	23	0.0 (-66.7,66.7)	24	0.0 (-33.3,66.7)	-1.19	0.234	21	0.0 (-66.7,33.3)	15	0.0 (-33.3,66.7)	-1.38	0.167
Insomnia	33.3	23	0.0 (-66.7,33.3)	0.0	24	0.0 (-33.3,66.7)	-0.48	0.635	22	0.0 (-66.7,33.3)	24	0.0 (-66.7,100.0)	0.12	0.907	22	0.0 (-66.7,66.7)	15	0.0 (-33.3,66.7)	-0.96	0.335
Appetite	0.0	23	0.0 (-66.7,100.0)	33.3	23	33.3 (-66.7,100.0)	-1.75	0.081	23	0.0 (-66.7,100.0)	24	0.0 (-33.3,66.7)	-0.80	0.421	22	0.0 (-33.3,100.0)	15	0.0 (-66.7,66.7)	0.12	0.904
Constipation	0.0	22	0.0 (-33.3,66.7)	0.0	24	0.0 (-33.3,33.3)	-0.64	0.525	22	0.0 (-33.3,33.3)	24	0.0 (-33.3,33.3)	-0.65	0.516	23	0.0 (-66.7,33.3)	15	0.0 (-33.3,33.3)	-0.66	0.511
Diarrhoea	0.0	23	0.0 (-33.3,33.3)	33.3	24	0.0 (-66.7,66.7)	0.42	0.678	22	0.0 (-33.3,66.7)	24	0.0 (-66.7,66.7)	0.03	0.980	23	0.0 (-33.3,33.3)	15	0.0 (-33.3,33.3)	-0.21	0.831
Financial	0.0	23	0.0 (-33.3,33.3)	0.0	23	0.0 (-33.3,100.0)	-1.12	0.262	23	0.0 (-33.3,66.7)	23	0.0 (-33.3,66.7)	-0.87	0.383	23	0.0 (-66.7,66.7)	14	0.0 (-66.7,33.3)	0.51	0.613
Panc Pain	8.3	23	0.0 (-33.3,33.3)	25.0	22	8.3 (-16.7,50.0)	-0.47	0.640	23	0.0 (-41.7,50.0)	23	0.0 (-33.3,50.0)	0.13	0.894	22	8.3 (-50.0,58.3)	15	0.0 (-33.3,75.0)	0.19	0.851
Bloating	0.0	23	0.0 (-33.3,33.3)	33.3	22	0.0 (-33.3,100.0)	-2.11	**0.035**	23	0.0 (-33.3,33.3)	23	0.0 (-66.7,66.7)	-0.62	0.536	22	0.0 (-66.7,100.0)	15	0.0 (-33.3,33.3)	0.42	0.674
Gastro	16.7	23	0.0 (-16.7,100.0)	33.3	22	8.3 (-50.0,66.7)	-0.36	0.718	23	0.0 (-66.7,66.7)	23	0.0 (-50.0,100.0)	0.35	0.726	22	0.0 (-66.7,66.7)	15	-16.7 (-50.0,50.0)	1.66	0.097

Taste	33.3	23	0.0 (-100.0,66.7)	33.3	22	0.0 (-33.3,100.0)	-0.91	0.361	23	0.0 (-66.7,66.7)	23	0.0 (-66.7,66.7)	-0.60	0.546	22	0.0 (-66.7,33.3)	15	0.0 (-66.7,33.3)	-0.34	0.732
Indigestion	0.0	22	0.0 (-33.3,100.0)	33.3	22	0.0 (-33.3,66.7)	0.11	0.915	21	0.0 (-100.0,66.7)	22	0.0 (-66.7,33.3)	1.17	0.244	22	0.0 (-66.7,100.0)	15	0.0 (0.0,33.3)	-0.45	0.651
Flatulence	33.3	23	0.0 (-33.3,100.0)	33.3	22	0.0 (-100,100)	-0.01	0.990	23	0.0 (-100.0,66.7)	23	0.0 (-66.7,33.3)	0.30	0.761	21	0.0 (-66.7,100.0)	14	0.0 (-33.3,33.3)	0.19	0.852
Weight	33.3	23	0.0 (-33.3,66.7)	33.3	22	0.0 (-66.7,66.7)	-1.02	0.310	22	0.0 (-66.7,66.7)	23	0.0 (-100,100)	-0.73	0.467	22	0.0 (-33.3,66.7)	15	0.0 (-66.7,66.7)	0.34	0.738
Weak limbs	33.3	23	0.0 (-66.7,33.3)	33.3	22	0.0 (-33.3,66.7)	-1.76	0.078	23	0.0 (-66.7,33.3)	23	0.0 (-33.3,100.0)	-1.37	0.169	21	0.0 (-33.3,33.3)	15	0.0 (-33.3,66.7)	-1.62	0.104
Dry mouth	33.3	22	0.0 (-66.7,33.3)	33.3	22	0.0 (-66.7,33.3)	-2.18	**0.029**	22	0.0 (-66.7,66.7)	22	0.0 (-66.7,100.0)	-1.23	0.220	22	0.0 (-66.7,0.0)	15	0.0 (-33.3,33.3)	-3.44	**0.001**
Jaundice	0.0	22	0.0 (-33.3,50.0)	0.0	21	0.0 (-50.0,33.3)	0.62	0.536	22	0.0 (-50.0,66.7)	22	0.0 (-33.3,16.7)	-0.05	0.956	19	0.0 (-66.7,50.0)	14	0.0 (-66.7,33.3)	-0.12	0.907
Bowel	33.3	23	0.0 (-33.3,66.7)	50.0	22	0.0 (-50.0,66.7)	1.02	0.306	23	0.0 (-50.0,66.7)	23	0.0 (-50.0,50.0)	-0.45	0.652	22	0.0 (-50.0,66.7)	15	0.0 (-33.3,50.0)	0.00	1.000
Image	33.3	23	0.0 (-33.3,50.0)	0.0	22	0.0 (-66.7,33.3)	0.51	0.608	23	0.0 (-50.0,50.0)	22	0.0 (-50.0,100.0)	-0.28	0.778	22	0.0 (-50.0,33.3)	15	0.0 (-16.7,66.7)	-2.29	**0.022**
Side effects	33.3	23	0.0 (-33.3,33.3)	33.3	22	0.0 (-33.3,66.7)	-0.55	0.584	23	0.0 (-66.7,33.3)	22	0.0 (-33.3,100.0)	-0.15	0.883	22	0.0 (-33.3,33.3)	15	0.0 (-33.3,33.3)	-0.02	0.987
Future	66.7	23	0.0 (-33.3,66.7)	33.3	22	0.0 (-66.7,100.0)	-0.32	0.747	23	0.0 (-33.3,66.7)	23	0.0 (-33.3,100.0)	-2.13	**0.033**	22	0.0 (-33.3,100.0)	15	0.0 (-66.7,66.7)	-0.52	0.600
Planning	33.3	23	0.0 (-33.3,66.7)	33.3	21	0.0 (-33.3,66.7)	0.20	0.841	23	0.0 (-100.0,66.7)	23	0.0 (-66.7,66.7)	-0.85	0.396	22	0.0 (-66.7,100.0)	15	0.0 (-33.3,66.7)	-0.80	0.426
Healthcare	100.0	23	0.0 (-100,100)	100.0	22	0.0 (-16.7,83.3)	-0.76	0.449	23	0.0 (-100.0,100.0)	23	0.0 (-33.3,50.0)	-0.25	0.803	22	0.0 (-100.0,16.7)	15	0.0 (-50.0,50.0)	-1.91	0.056
Sexual	41.7	20	0.0 (-66.7,66.7)	66.7	16	0.0 (-100.0,83.3)	-0.07	0.941	20	0.0 (0.0,66.7)	18	0.0 (-100.0,83.3)	1.24	0.213	17	0.0 (-33.3,33.3)	13	0.0 (-100.0,83.3)	-0.55	0.583

NB: Negative differences in functioning scales (and SatHC) represent HRQL worsening whereas negative differences in symptom scores represents HRQL improvement. Abbreviations as shown in Table 1. P values < 0.05 are in bold.

Table 6. Mean week 23 QLQ-PAN26 scale scores by those with and without any CTCAE grade 3 or 4 adverse events during CRT

PAN 26 scale	No grade 3 or 4 adverse events during CRT				Any Grade 3 or 4 adverse events during CRT			
	n	Mean	Lower 95% CI	Upper 95% CI	n	Mean	Lower 95% CI	Upper 95% CI
Pancreatic pain*	38	23.90	16.93	30.88	10	36.67	18.20	55.14
Bloating*	38	20.18	11.52	28.83	10	36.67	15.79	57.55
Gastrointestinal*	38	32.89	21.40	44.39	10	58.33	35.68	80.99
Taste loss	38	34.21	24.19	44.24	10	40.00	10.69	69.31
Indigestion	38	21.05	11.38	30.73	10	23.33	0.71	45.95
Flatulence	38	45.61	34.98	56.25	10	50.00	26.83	73.17
Weight*	38	31.58	20.20	42.96	10	63.33	32.65	94.01
Weak limbs*	38	26.32	17.43	35.20	10	53.33	30.30	76.37
Dry mouth	37	28.83	18.63	39.03	10	23.33	3.70	42.96
Jaundice	38	7.89	2.84	12.95	10	8.33	2.05	14.62
Altered bowel habit*	38	28.51	18.41	38.61	10	58.33	33.67	82.99
Poor body image	38	25.44	14.80	36.07	10	25.00	3.05	46.95
Side effects of treatment	38	35.96	27.37	44.56	10	36.67	12.95	60.38
Future health concern*	38	51.75	39.89	63.62	10	73.33	48.71	97.96
Forward planning limited*	37	33.33	21.91	44.75	10	56.67	37.04	76.30
Satisfaction with healthcare	38	92.11	85.52	98.69	10	91.67	81.53	101.80
Sexual dissatisfaction	31	59.14	43.45	74.83	7	66.67	32.20	101.13

*indicates a difference in means of more than 10 points