



The Quality of Life in Neoadjuvant vs Adjuvant Therapy of Esophageal Cancer Treatment Trial



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Background

- The ideal treatment of resectable esophageal cancer remains unknown.
- Most centres have used neoadjuvant cisplatin and 5FU with radiation followed by surgery.
- Our centre has been using adjuvant epirubicin, cisplatin, and 5 FU chemotherapy with extended field radiation that includes the anastomosis with encouraging results.
- We hypothesized that both tri-modality treatment options would provide similar survival results but may have different patient centred experiences with respect to quality-of-life and adverse events.

Objective

We compared the health-related quality-of-life (HRQOL) using the FACT-E between 2 tri-modality treatment protocols for resectable esophageal cancer.

Methods

- Prospective, concealed, and centrally randomized trial from April 2009 to November 2016.
- NCT 00907543

Population:

- Sequential patients with stage I to III resectable cancer of the esophagus in London, Canada.

Control (N)

- Standard 2 cycles neoadjuvant cisplatin 25 mg/m² days 1-4 and 5-FU 1,000 mg/m² daily x 4 for 2 cycles q 28 days, concurrent with 50.4 Gy radiotherapy followed by surgical resection.

Intervention (A)

- Surgical resection followed by adjuvant epirubicin 50 mg/m², cisplatin 60 mg/m², 5-FU 200 mg/m² infusion daily q 21 x 2 cycles, then cisplatin 60 mg/m², 5-FU 200 mg/m² infusion daily q 21 x 2 cycles with concurrent 50.4 Gy extended volume (including the anastomosis) radiotherapy.

Outcomes

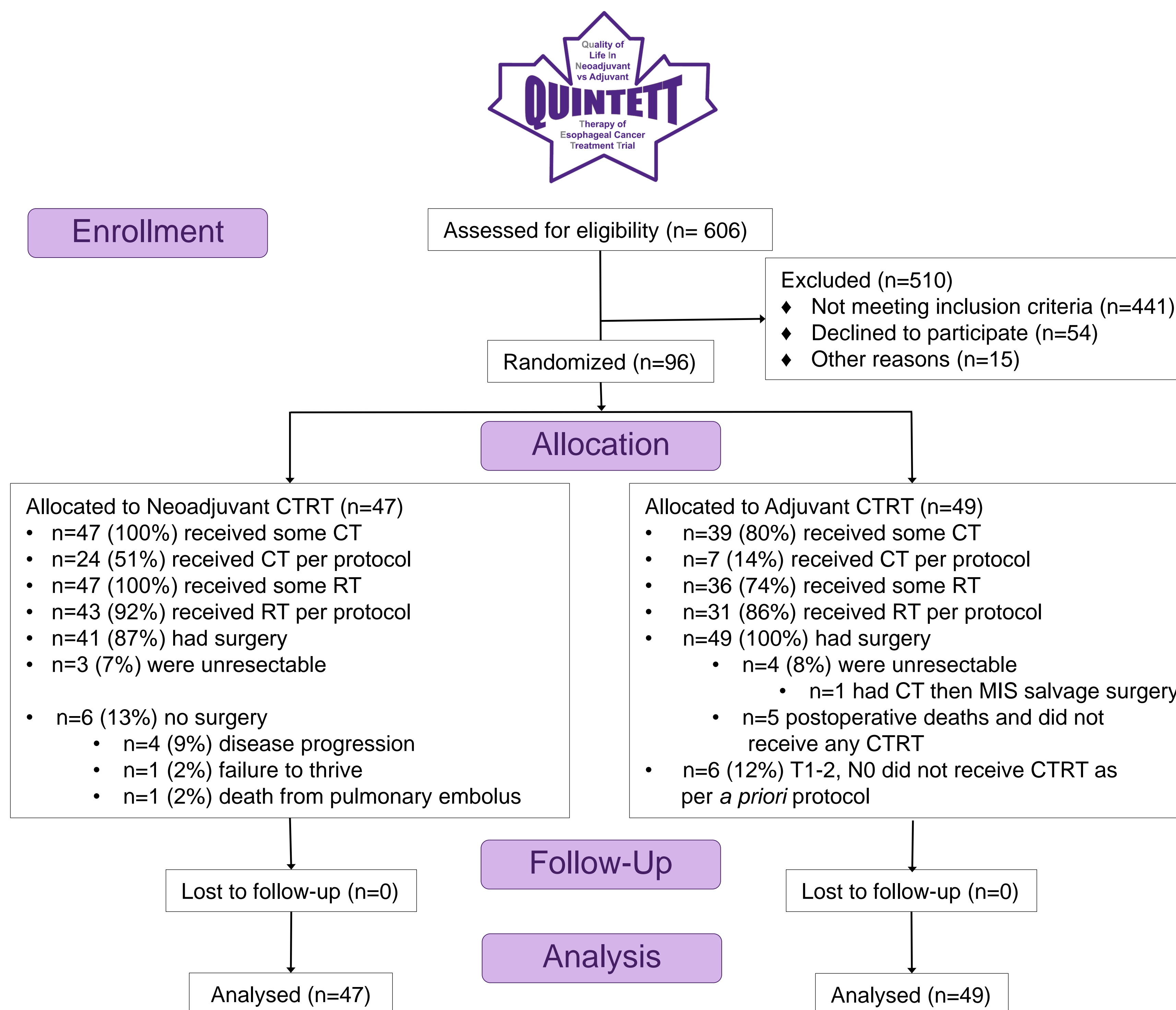
- Primary Outcome: HRQOL using the FACT-E at one year. *A priori* minimal important difference was 15.
- Secondary Outcomes: FACT-G, EORTC-OG25, EQ5D; Overall survival; Disease-free survival; Adverse events CTCAE 4

Analysis

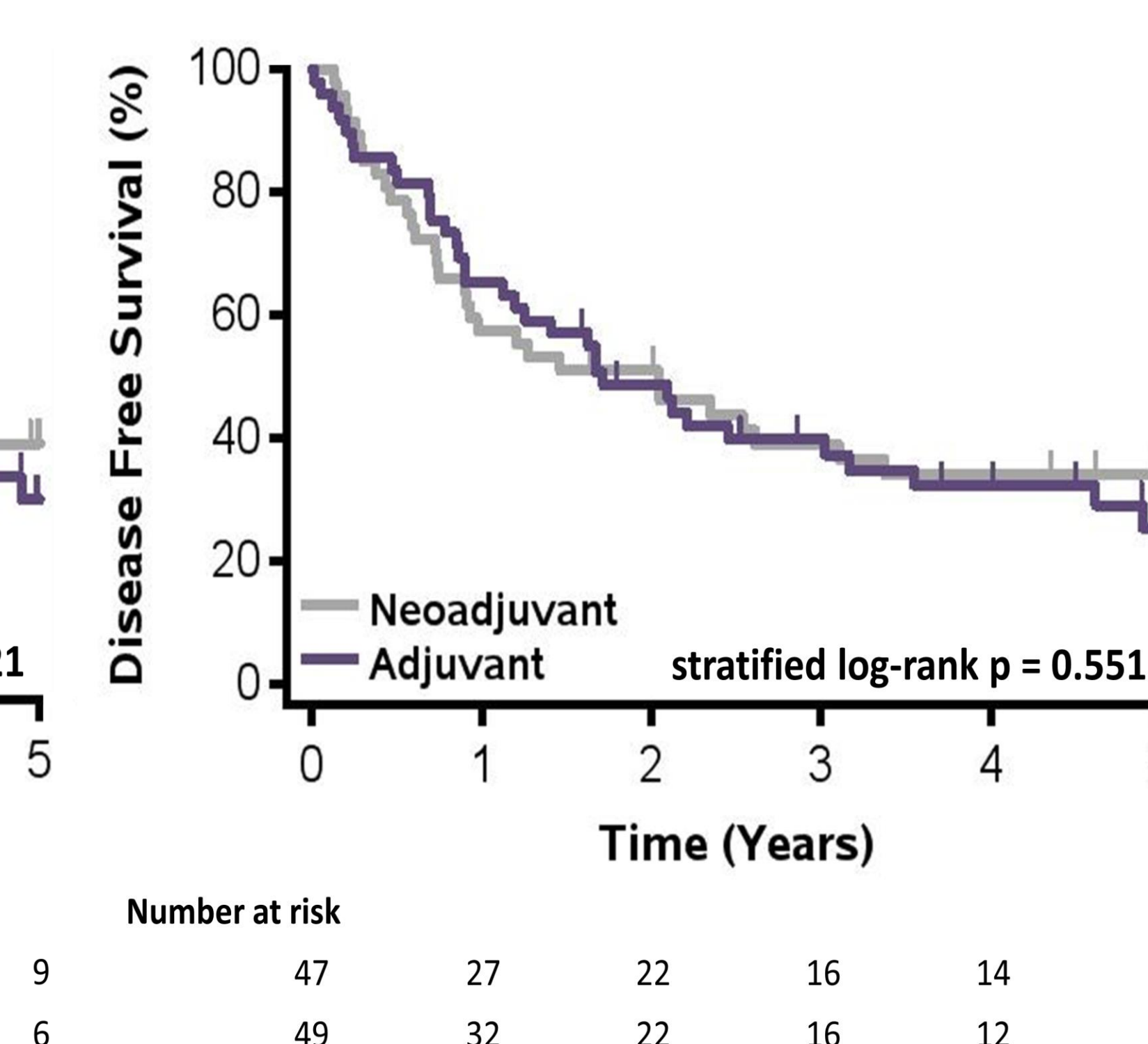
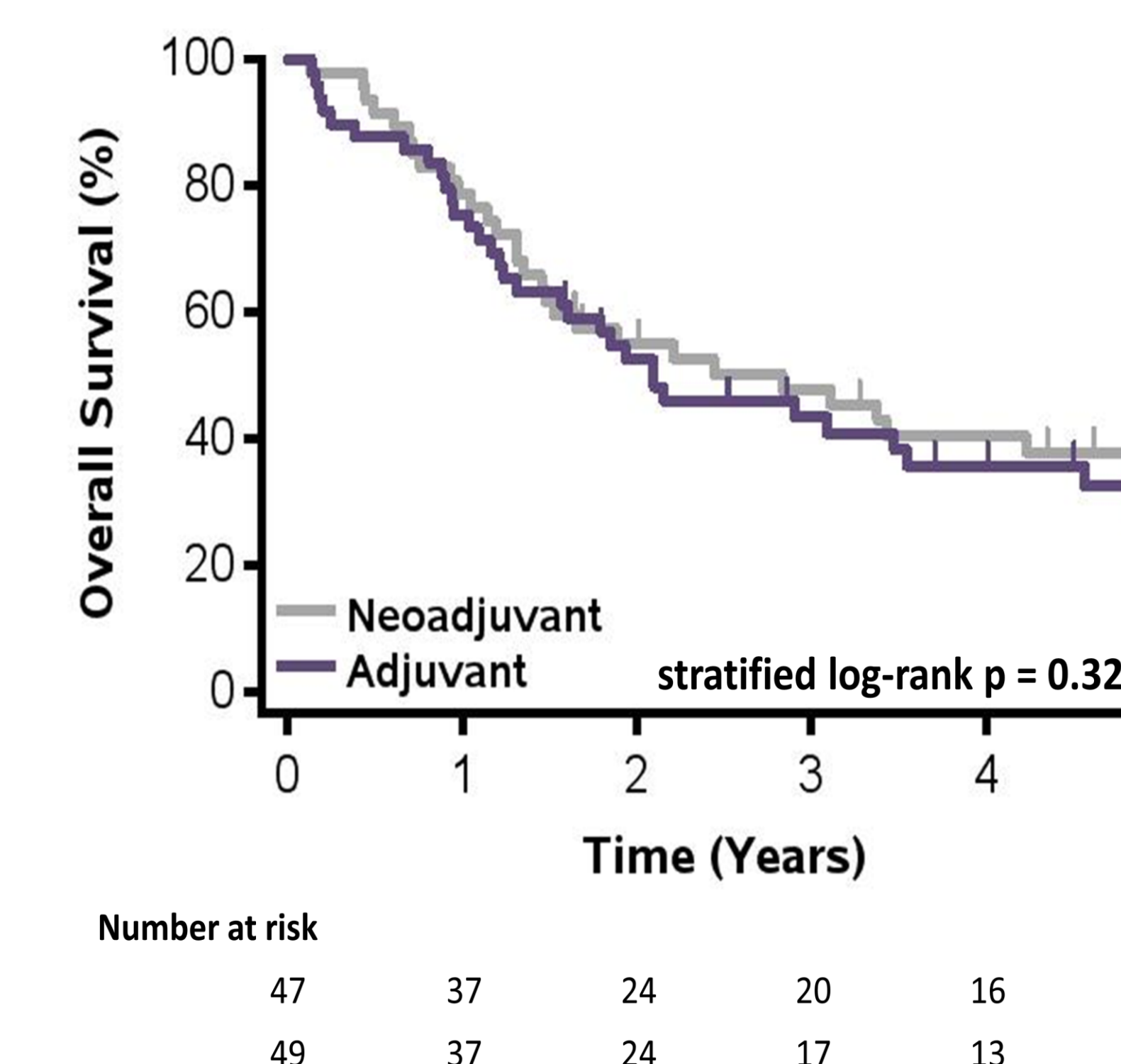
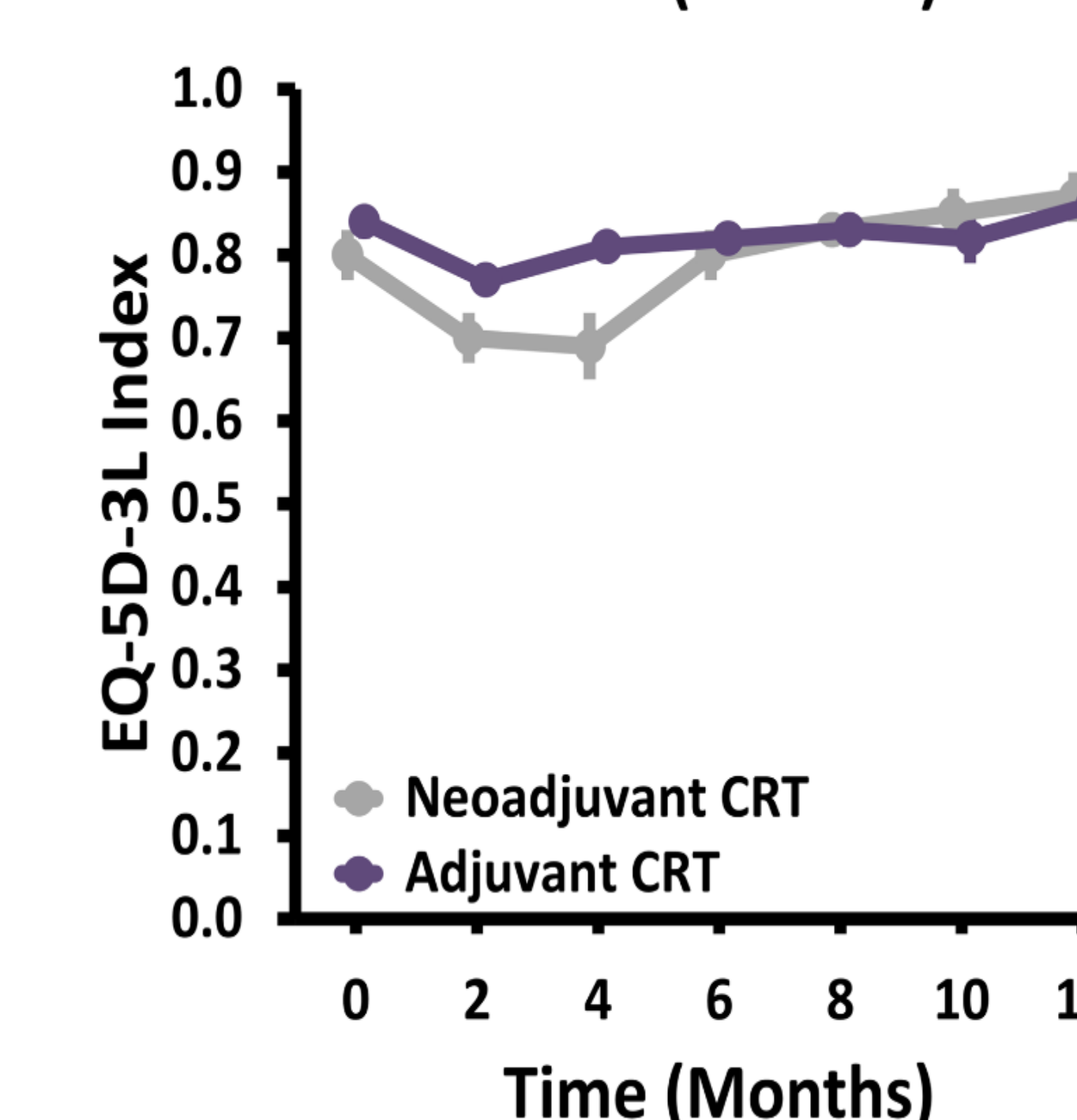
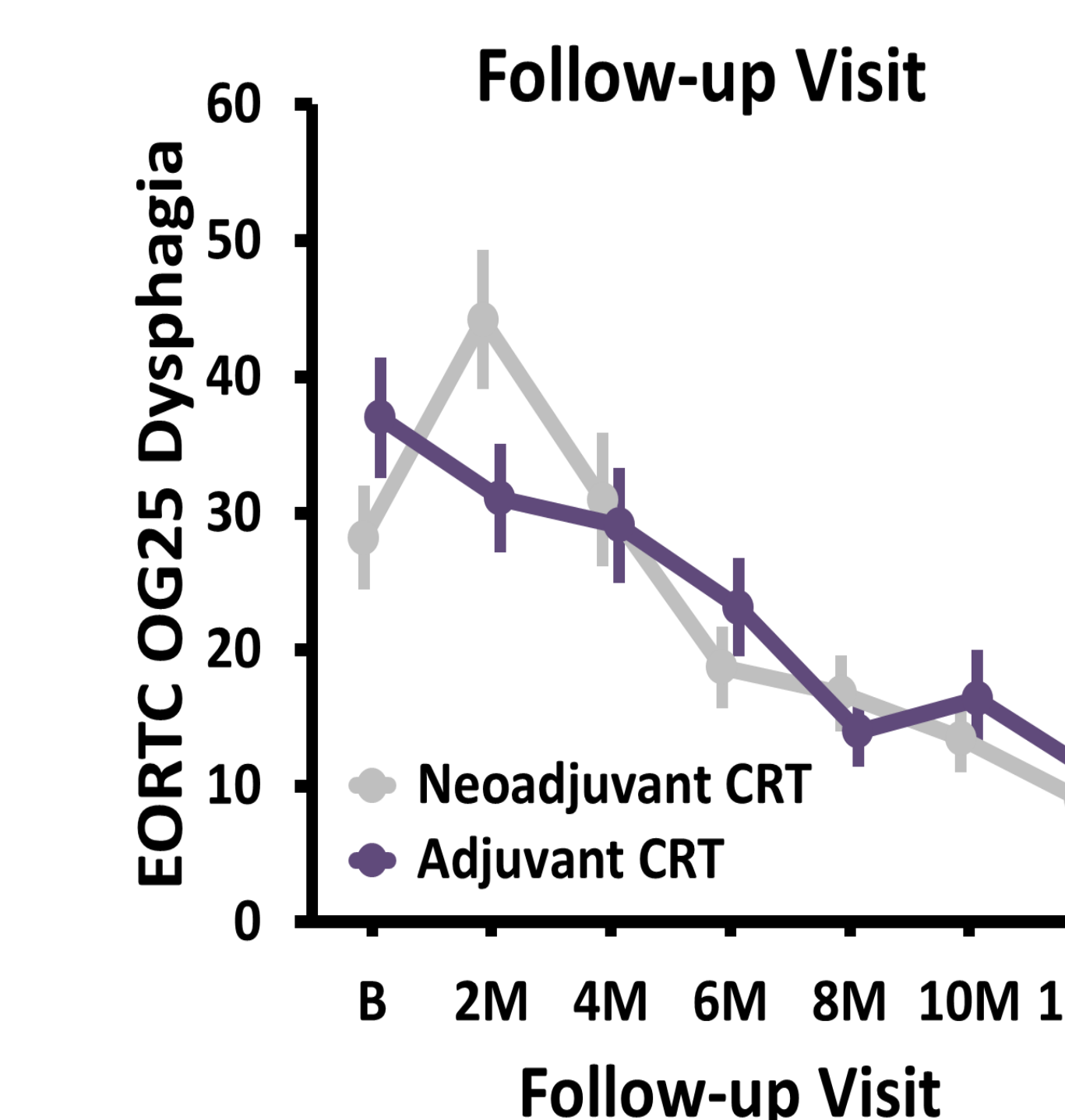
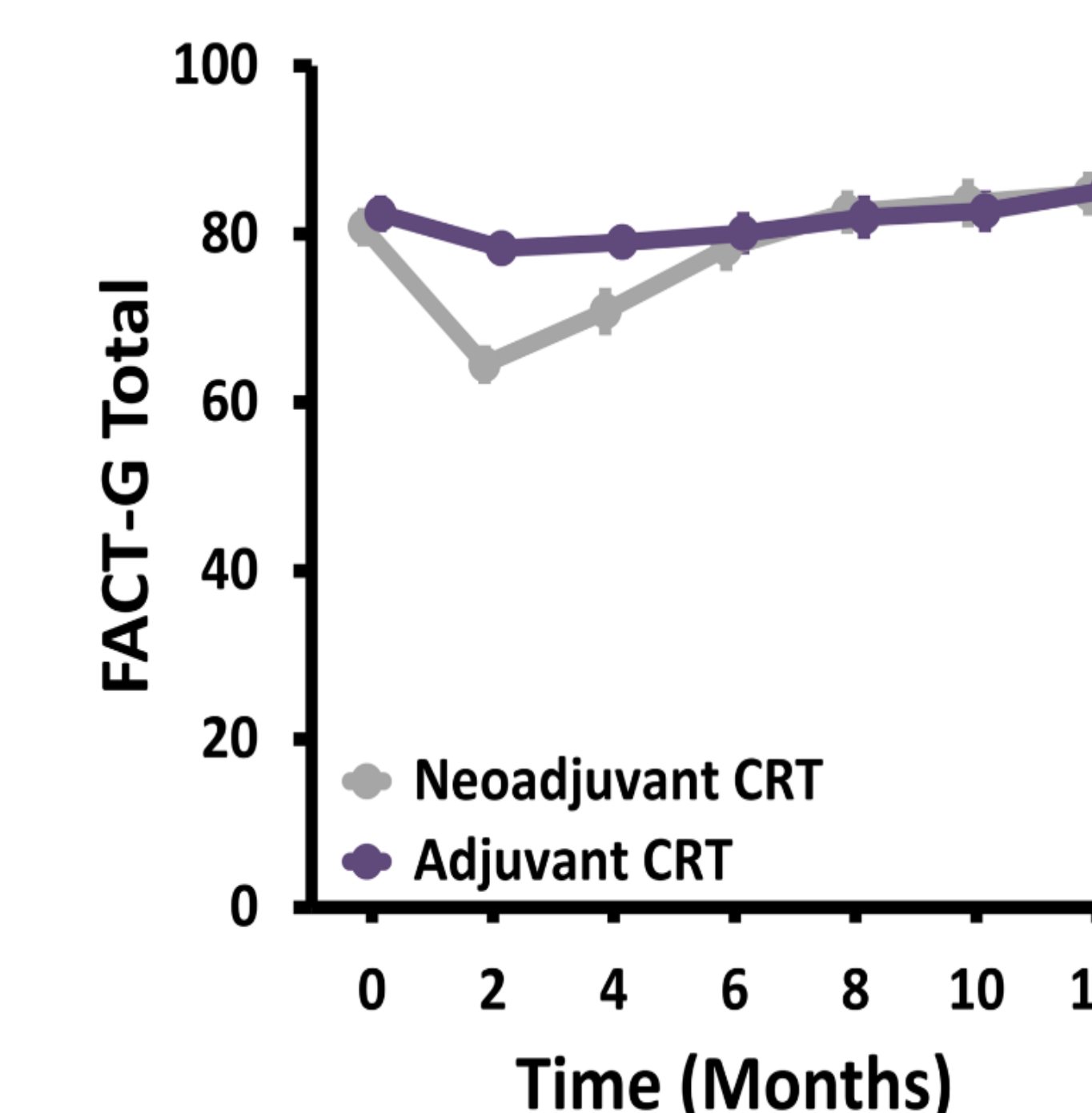
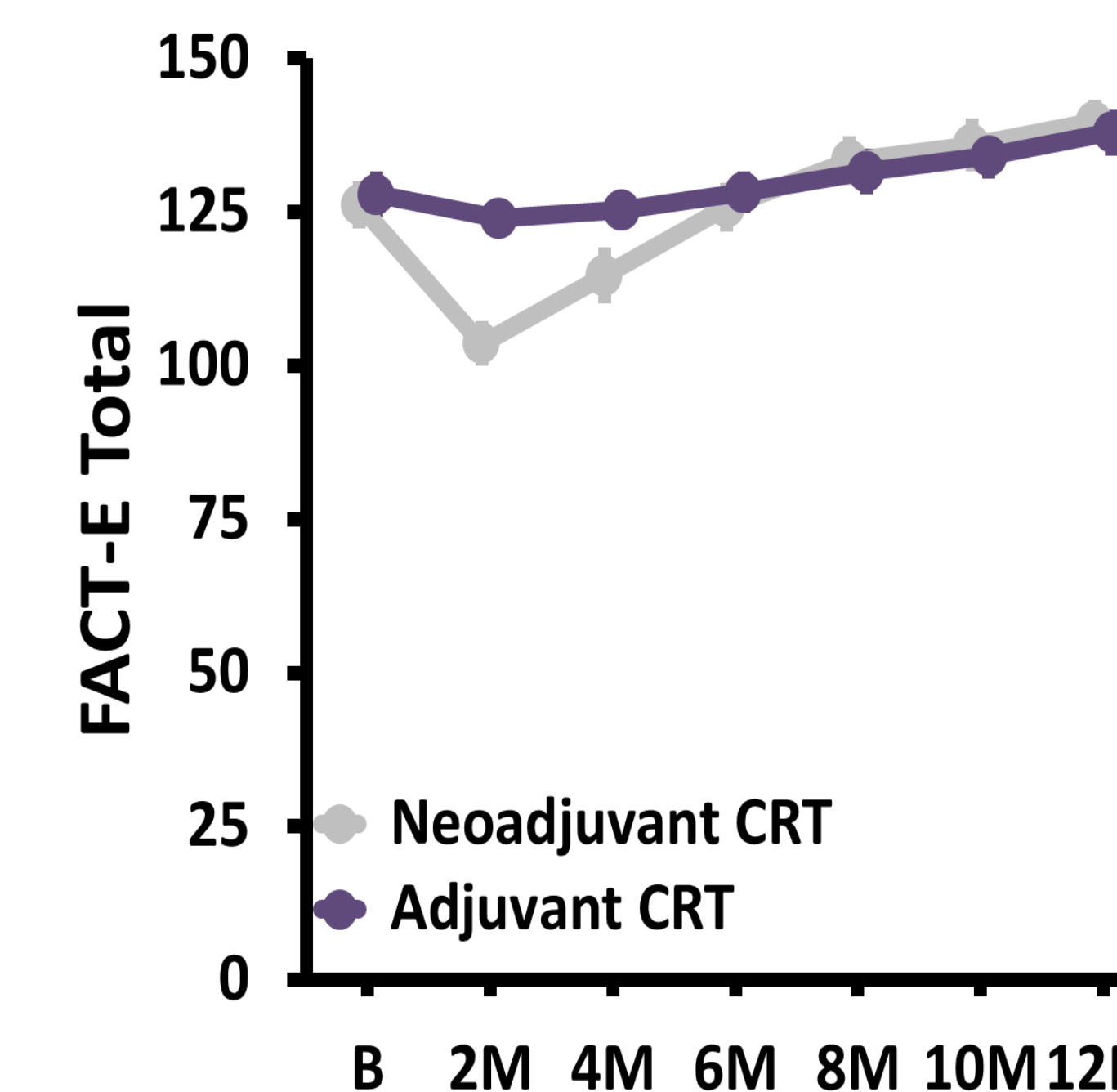
- Intention-to-treat analysis using the chi-square test, Fisher's exact test, two-sample T-test, Wilcoxon rank sum test or paired T-test (compared to baseline) as appropriate.
- Kaplan-Meier estimates and Log-rank test stratified by clinical nodal status using SAS version 9.4 software using two-sided statistical testing at the 0.05 significance level.

Results

- Baseline characteristics were well matched between arms.
- The median follow-up was 5.0 years [95% CI :4.6 to 5.5].
- The combined stage distribution was: I 9%; II 22%; III 58%; TxN0-1 10%.
- There was no significant difference in the FACT-E total scores between arms at one year (p=0.759), with (N) 35.5% vs. (A) 41.2% respectively showing an increase of ≥ 15 points compared to pre-treatment (p=0.638).
- The HRQOL was temporarily significantly inferior at 2 months in the N arm for FACT-E, EORTC-OG25, and EQ-5D-3L in the dysphagia, reflux, pain, taste, and coughing domains (p<0.05).**
- 51% of patients were able to complete the prescribed N arm chemotherapy without modification compared to only 14% in the A arm (p<0.001).
- Chemoradiotherapy adverse events significantly more frequent in the N arm (p<0.05).
- Overall surgery related adverse events were similar between arms.



Characteristic	Neoadjuvant CRT (n=47)	Adjuvant CRT (n=49)	p-value
Age – mean ± SD	63.1 ± 7.7	65.6 ± 8.0	0.112
Gender – Male n(%)	41 (87.2)	37 (75.5)	0.141
Histology – n(%)			
Adenocarcinoma	38 (80.9)	43 (87.8)	0.039
Squamous	2 (4.3)	5 (10.2)	
Unknown	7 (14.9)	1 (2.0)	
Type of surgery – n (% minimally invasive)	30(64)	39(80)	-
Mostly laparoscopic transhiatal – n(%)	25(53)	30(61)	-
Neck anastomoses – n(%)	32(68)	40(82)	-
30-Day Mortality	0	0	-
90-Day Mortality – n(%)	1 (2.1)	5 (10.2)	0.204
5 year overall survival – % [log rank]	37.9	28.9	0.321
5-year disease free survival – % [log rank]	34.0	25.5	0.551
Adverse Events – n(%)			
Chemoradiotherapy + Grade ≥ 2	47 (100)	34 (69.4)	< 0.001
Chemoradiotherapy + Grade ≥ 3	37 (78.7)	27 (55.1)	0.014
Surgery + Grade ≥ 2	34 (72.3)	42 (85.7)	0.107
Surgery + Grade ≥ 3	27 (57.5)	37 (75.5)	0.061



Conclusions

- Neoadjuvant cisplatin, 5FU chemotherapy with radiation followed by surgery and adjuvant epirubicin, 5FU, cisplatin chemotherapy with extended field radiation tri-modality therapy are both challenging and provide similar survival benefits but different health-related quality-of-life experiences for patients with resectable esophageal cancer.
- Less toxic protocols are needed.

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