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Neoadjuvant camrelizumab and chemotherapy in patients with resectable esophageal squamous cell carcinoma: A prospective, single-arm, open-label study

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Abstract

Background. Esophageal cancer (EC) is a major cause of cancer-related deaths worldwide, bringing tremendous pressure to the healthcare system and patients. Esophageal squamous cell carcinoma (ESCC) is the main subtype of EC in the Chinese population.

Objectives. This study aimed to extend the neoadjuvant therapy cycle to 4 cycles and evaluate the efficacy and safety of neoadjuvant camrelizumab combined with chemotherapy for the treatment of resectable ESCC.

Materials and methods. The enrolled patients received neoadjuvant camrelizumab (200 mg, day 1), nab-paclitaxel (260 mg/m^2, day 1) and carboplatin (area under curve; 5 mg/mL/min) every 21 days for 4 cycles, and surgery was performed within 4–6 weeks after the first day of the 4th treatment cycle. The primary endpoint of the study was the pathological complete response (pCR) rate.

Results. From December 15, 2021, to October 1, 2022, a total of 35 patients were enrolled in the study. All patients completed the full 4-cycle treatment and were deemed fit for surgical intervention. Thirty-four (97.1%) patients achieved R0 resection, 18 (51.4%) showed a pCR rate, and 27 (77.1%) achieved a major pathological response (MPR). Tumor degradation was observed in 30 out of 35 patients (85.7%). Multivariate logistic regression analyses further confirmed that age (odds ratio (OR) = 6.710, 95% confidence interval (95% CI): 3.512–44.403) and programmed death-ligand 1 (PD-L1) (OR = 2.855, 95% CI: 1.181–3.079) were independent predictors of pCR. The most prevalent adverse event (AE) was leukopenia, which was experienced by 23 out of 35 patients (65.7%). Grade 3 or higher AEs included leukopenia in 2 cases (5.7%) and neutropenia in 12 cases (34.3%). No delays in surgery were observed.

Conclusions. As demonstrated in this study, the 4 cycles of camrelizumab combined with nab-paclitaxel and carboplatin, which exhibited a relatively high pCR rate and acceptable safety, suggest a strong rationale for its further evaluation in resectable ESCC.

Key words: esophageal squamous cell carcinoma (ESCC), neoadjuvant therapy, anti-programmed death-1 (PD-1), camrelizumab

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Background

Esophageal cancer (EC) is a major cause of cancer-related deaths worldwide, bringing tremendous pressure to the healthcare system and patients.[1–3] Esophageal cancer primarily consists of 2 different epidemiological and pathological diseases, namely esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma.[4] Esophageal squamous cell carcinoma is the main subtype of EC in the Chinese population.[5,6] Surgery remains the primary treatment for resectable ESCC, but up to 50% of patients fail to achieve R0 resection, resulting in early postoperative recurrence.[7] Neoadjuvant chemoradiotherapy followed by surgery is a widely used standard treatment for patients with resectable EC.[8,9] In a study of preoperative chemoradiotherapy (carboplatin, paclitaxel and radiotherapy), known as Chemoradiotherapy for EC followed by Surgery Study (CROSS), there was an overall improvement in survival lasting at least 10 years in patients with locally advanced resectable EC.[10,11] However, the long-term clinical outcomes of neoadjuvant chemoradiotherapy remain unsatisfactory because death still occurs in more than half of patients.[10] Moreover, the perioperative toxicities caused by chemoradiation reduce its attractiveness to patients.[12] Therefore, clinicians and ESCC patients urgently need a neoadjuvant regimen that is more effective and less toxic.

Preclinical studies have shown that the combination of programmed cell death 1 (PD-1) inhibitors and chemotherapy can further strengthen the host immune response and prevent cancer cell escape.[13] In previous studies, the majority of neoadjuvant PD-1 antibody-combined therapy involved 2 cycles, while 4 cycles of neoadjuvant PD-1 antibody-combined therapy are rarely used.[14] Lv et al. reported that 3–4 cycles of neoadjuvant sintilimab, an immune checkpoint inhibitor targeting PD-1, plus chemotherapy in resectable locally advanced ESCC have a higher pathological complete response (pCR) rate than only 2 cycles of neoadjuvant sintilimab plus chemotherapy (47.9% compared to 12.5%; p = 0.0003).[15] This suggests that extending the neoadjuvant therapy cycle may increase the pCR rate, which is associated with prolonged overall survival (OS).[16,17] Camrelizumab, a product developed in China, is a novel IgG4-kappa anti-PD-1 inhibitor that has been administered in the treatment of many types of malignancies.[18] Two cycles of neoadjuvant camrelizumab combined with chemotherapy have been shown to be effective and tolerable in newly diagnosed resectable ESCC, achieving pCR in 25% of patients.[19] Thus, although using 2 cycles of neoadjuvant therapy has been successful, 75% of patients still do not achieve pCR. Therefore, the extension of the camrelizumab-combined therapy cycle in patients with resectable locally advanced ESCC is worth exploring.

Objectives

This study aimed to extend the neoadjuvant therapy cycle to 4 cycles and evaluate the efficacy and safety of neoadjuvant camrelizumab combined with chemotherapy for the treatment of resectable ESCC, hoping to develop a more effective regimen to enhance the clinical outcomes of ESCC patients.

Materials and methods

Study design and participants

In this prospective, single-arm study, we compared the efficacy and safety in a group of ESCC patients receiving 4 cycles of neoadjuvant camrelizumab-combined therapy with a group of historical controls who received only 2 cycles of neoadjuvant camrelizumab-combined therapy. The flowchart for the study is presented in Fig. 1. The study was conducted from December 15, 2021, to October 1, 2022, at the People's Hospital of Yangzhong (China). The inclusion criteria were as follows: 1) histologically confirmed resectable (stage II or III) ESCC; 2) male or female patients; 3) aged 18–75 years; 4) with an Eastern Cooperative Oncology Group (ECOG) score of 0 or 1. The exclusion criteria were as follows: 1) severe disease within the previous 5 years; 2) prior history of anti-PD-1 or anti-programmed death-ligand 1 (anti-PD-L1) treatment; 3) prior history of interstitial lung disease or active non-infectious pneumonia; 4) treatment with corticosteroids or other immunosuppressants in the preceding 2 weeks. The expression of the PD-L1 biomarker was not considered in the enrolled patients.

All patients provided written informed consent before enrollment, and the study was approved by the ethics committee of the People's Hospital of Yangzhong (approval No. 2021142). All patients enrolled in this experiment were Chinese.

Procedures

All patients underwent clinical evaluation, including upper gastrointestinal endoscopy with diagnostic biopsy, computed tomography (CT) of the chest, ultrasonography of the major organs, routine electrocardiogram, echocardiography, pulmonary function test, and radionuclide bone scintigraphy. Before undergoing surgical resection, patients were treated with 4 cycles of the following drugs intravenously: camrelizumab (200 mg on day 1 every 3 weeks), nab-paclitaxel (260 mg/m^2 on day 1 every 3 weeks) and carboplatin (area under the curve of 5 mg/mL/min on day 1 every 3 weeks).

After the completion of neoadjuvant therapy, a reassessment was conducted to exclude patients with surgical contraindications. The reassessment included the same

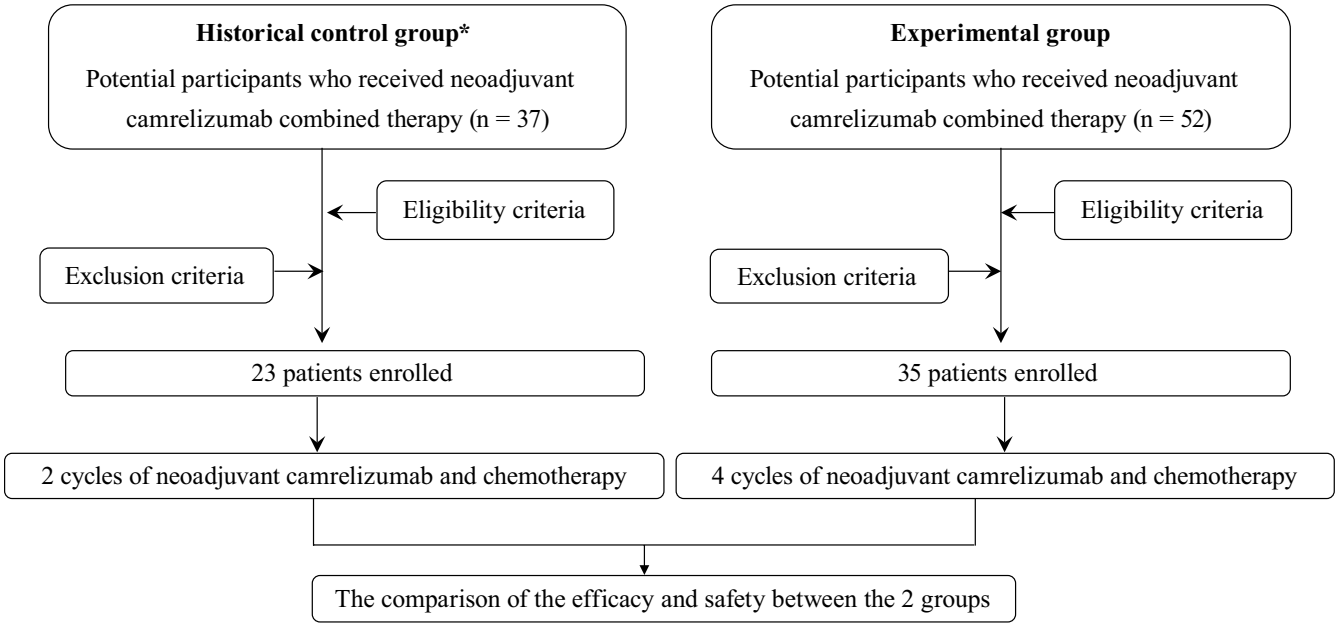

Fig. 1. Study flowchart based on the study by Yang et al.[17]

tests as the pretreatment staging. Surgery was scheduled to be performed within 4–6 weeks after the 1st day of the 4th treatment cycle. McKeown or Ivor Lewis esophagectomy was performed according to standard institutional procedures, including double-field lymphadenectomy and total mediastinal lymphadenectomy.

Outcomes

The primary endpoint of this study was pCR, defined as no residual tumor cells. The secondary endpoints included major pathological response (MPR), defined as <10% residual tumor cells, R0 resection rate, objective response rate (ORR), disease control rate (DCR), disease-free survival (DFS, calculated from the date of enrollment), overall survival (OS), and safety. According to the Response Evaluation Criteria in Solid Tumors (RECIST) v. 1.1, the target lesion of EC was defined as lymph nodes with a small diameter (≥15 mm); the primary esophageal lesion was not considered the target lesion. Tumor response was evaluated every 2 cycles. Toxicity profiles were evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) (v. 5.0).

Statistical analyses

According to a previous study,[17] the pCR rate of 2 cycles of neoadjuvant therapy was 25%, while 50% was the expected rate in our study. The sample size ensuring a higher pCR rate was calculated using PASS 15 software (NCSS LCC, Kaysville, USA). A total of 30 eligible subjects would be required to detect a difference between 25% and 50% pCR rate with a power of 80%. Considering a 15% patient loss, at least 35 cases would need to be enrolled. Categorical variables, including gender, smoking status, tumor location, ECOG performance status, alcohol consumption, clinical tumor stage, clinical nodal stage, clinical TNM stage, histologic grade, and PD-L1, were presented as frequency count (percentage), and numerical variables were presented as median (interquartile range (IQR)) or mean ± standard deviation (M ±SD). Survival probability was evaluated using the Kaplan–Meier method. Multivariate logistic regression analysis was performed to explore the independent predictors of pCR. The goodness of fit was assessed using Nagelkerke R^2. Multicollinearity was checked using the variance inflation factor (VIF); the VIF values of all independent predictors were less than 2. All reported p-values were bilateral, with $p < 0.05$ considered statistically significant.

Results

Baseline

From December 15, 2021, to October 1, 2022, a total of 52 patients from the People's Hospital of Yangzhong were screened as eligible for the experimental group. Thirty-five patients were enrolled after providing informed consent (Fig. 1). As seen in Table 1, 19 patients (54.3%) in the experimental group were under 65 years old, and 16 (45.7%) patients were over 65 years old. Among all the patients, 71.4% were male (25 patients) and 28.6% were female (10 patients). Most of the patients (54.3%) were former or current smokers. The tumors were located in the upper segment (11.4%), middle segment (45.7%) and lower segment (42.9%) of the esophagus. Before treatment, T3 (62.9%) was the predominant clinical tumor

Table 1. Baseline characteristics of the patients

Characteristic		Experimental group (n = 35)	Historical control group* (n = 23)
Age, n (%) [years]	≤65	19 (54.3)	N/A
	>65	16 (45.7)	N/A
Gender, n (%)	male	25 (71.4)	22 (95.7)
	female	10 (28.6)	1 (4.3)
ECOG performance status, n (%)	0	27 (77.1)	21 (91.3)
	1	8 (22.9)	2 (8.7)
Smoking status, n (%)	never	16 (45.7)	7 (30.4)
	former or current	19 (54.3)	16 (69.6)
Alcohol consumption, n (%)	never	14 (40.0)	11 (47.8)
	former or current	21 (60.0)	12 (52.2)
Tumor location, n (%)	upper segment	4 (11.4)	1 (4.3)
	middle segment	16 (45.7)	9 (39.1)
	lower segment	15 (42.9)	13 (56.5)
Clinical tumor stage, n (%)	T1	7 (20.0)	N/A
	T2	4 (11.4)	N/A
	T3	22 (62.9)	N/A
	T4	2 (5.7)	N/A
Clinical nodal stage, n (%)	N0	6 (17.1)	N/A
	N1	23 (65.7)	N/A
	N2	6 (17.1)	N/A
Clinical TNM stage, n (%)	II	13 (37.1)	8 (34.8)
	III	22 (62.9)	15 (65.2)
Histologic grade, n (%)	well differentiated	6 (17.1)	N/A
	moderately differentiated	8 (22.9)	N/A
	poorly differentiated	21 (60.0)	N/A
PD-L1, CPS, n (%)	<1	17 (48.6)	7 (30.4)
	≥1	18 (51.4)	12 (52.2)

ECOG – Eastern Cooperative Oncology Group; TNM – tumor node metastasis; PD-L1 – programmed death-ligand 1; CPS – combined positive score; N/A – not applicable; * based on the results obtained by Yang et al.[17]

stage, while N1 (65.7%) was the most common clinical nodal stage. Thirteen patients (37.1%) had stage II tumors and 22 patients (62.9%) had stage III tumors. Twenty-seven patients (77.1%) had an ECOG performance score of 0 and 8 patients (22.9%) had a score of 1. The PD-L1 expression was evaluated in the biopsy samples. The results showed that 18 samples (51.4%) were PD-L1-positive (combined positive score (CPS) ≥ 1) and 17 samples (48.6%) were PD-L1-negative (CPS < 1). Tumors were determined to be well differentiated in 6 patients (17.1%), moderately differentiated in 8 patients (22.9%) and poorly differentiated in 21 patients (60.0%). Overall, there were slightly more female patients in the experimental group than in the historical control group, and there were also more patients with an ECOG performance score of 1 in the experimental group. The baseline characteristics of the 35 patients in the experimental group and the 23 patients in the historical control group are summarized in Table 1.

Tumor response

Following a course of 4 cycles of neoadjuvant immunotherapy in combination with chemotherapy, 28 patients with target lesions were evaluable for response in the experimental group. Two patients (7.1%) achieved complete response, 25 patients (89.3%) showed partial response, 1 patient (3.6%) remained stable, and no patients had progressive disease, resulting in an ORR of 96.4% and a DCR of 100.0% (Table 2 and Fig. 2). In the historical control group, the ORR and DCR were 90.5% and 100.0%, respectively. The details of these outcomes are presented in Table 2.

Surgical and pathological outcomes

In the experimental group, 35 patients underwent surgery, with 34 (97.1%) achieving R0 resection, 18 (51.4%) showing pCR and 27 (77.1%) achieving MPR (Table 3).

Table 2. Tumor response

Variable		Experimental group (n = 28)	Historical control group* (n = 21)
Best overall response, n (%)	complete response	2 (7.1)	1 (4.8)
	partial response	25 (89.3)	18 (85.7)
	stable disease	1 (3.6)	2 (9.5)
Progressive disease		0	0
Objective response rate, n (%)		27 (96.4)	19 (90.5)
Disease control rate, n (%)		28 (100.0)	21 (100.0)

* based on the results obtained by Yang et al.[17]

Table 3. Surgical and pathological outcomes

Characteristics		Experimental group (n = 35)	Historical control group* (n = 20)
Successful R0 resection, n (%)		34 (97.1)	20 (100)
Pathological response, n (%)	pCR	18 (51.4)	5 (25.0)
	MPR	27 (77.1)	10 (50.0)
Downstaging of TNM stage, n (%)	yes	30 (85.7)	13 (65.0)
	no	5 (14.3)	7 (35.0)
Blood loss (mL), median (IQR)		100.0 (65.0–185.0)	N/A
Cumulative operative time (min), M ±SD		265.9 ±46.7	292.5 ±53.1
Postoperative hospital stay [days], median (IQR)		21.0 (20.0–25.0)	N/A
Surgical complications, n (%)	anastomotic leakage	1 (2.9)	2 (10.0)
	pulmonary infection	2 (5.7)	1 (5.0)
	incisional hernia	1 (2.9)	N/A
	postoperative bleeding	1 (2.9)	1 (5.0)
	postoperative hoarseness	1 (2.9)	1 (5.0)

pCR – pathological complete response; MPR – major pathological response; M ±SD – mean ± standard deviation; TNM – tumor node metastasis; IQR – interquartile range; N/A – not applicable; * based on the results obtained by Yang et al.[17]

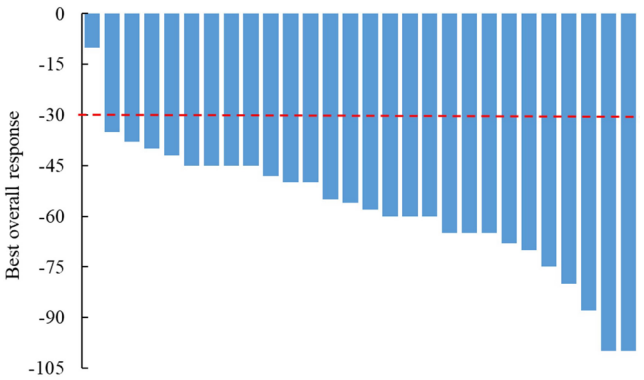

Fig. 2. Bar plot of the best overall response in the population (n = 28) according to RECIST1.1. Each bar represents 1 patient

Tumor degradation was observed in 30 out of 35 patients (85.7%). The median intraoperative blood loss was 100.0 mL (IQR: 65.0–185.0 mL), and the average operative time was 265.9 ±46.7 min. The median hospital stay after surgery was 21.0 days (IQR: 20.0–25.0). Table 3 summarizes the postoperative complications, which included 1 case each of anastomotic leakage, incisional hernia, heavy bleeding, and hoarseness, and 2 cases of pulmonary infection (5.7%). No serious complications, such as respiratory failure, heart failure, deep vein thrombosis, or acute respiratory distress syndrome, were reported. The proportions of patients achieving pCR, MPR and downstaging of the tumor node metastasis (TNM) stage were higher in the experimental group than in the historical control group, and the pCR rate improved by 26.4%. The incidence of surgical complications was low in both groups. The details are listed in Table 3.

Exploratory analysis

To further clarify the relationship between the baseline characteristics and pCR in patients with resectable ESCC, the Box–Tidwell test was conducted. Its results revealed a linear relationship between all continuous independent variables and the dependent variable logit conversion value (all $p > 0.05$) (Supplementary Table 1). Next, we performed a multivariate logistic regression analysis and confirmed that age (OR = 6.710, 95% CI: 3.512–44.403) and PD-L1 CPS (OR = 2.855, 95% CI: 1.181–3.079) were independent predictors of pCR (Table 4), indicating that the drug was more effective for patients aged <65 years and with a higher expression of PD-L1 (Nagelkerke $R^2 = 0.676$, $p = 0.010$).

Table 4. Multivariate analyses for pathological complete response (PCR) in patients with resectable esophageal squamous cell carcinoma in the experimental group

Variable		OR (95% CI)	p-value
Age [years]	>65	reference	
	≤65	6.710 (3.512, 44.403)	0.016
Gender	male	reference	
	female	1.510 (0.022, 15.010)	0.842
ECOG performance status	0	reference	
	1	0.315 (0.008, 6.843)	0.475
Smoking status	never	reference	
	former or current	0.163 (0.002, 4.553)	0.322
Alcohol consumption	never	reference	
	former or current	1.373 (0.091, 26.837)	0.819
Tumor location	upper segment	reference	
	middle segment	6.798 (0.075, 18.282)	0.430
	lower segment	1.924 (0.020, 3.485)	0.780
Histologic grade	well differentiated	reference	
	moderately differentiated	0.070 (0.002, 2.910)	0.221
	poorly differentiated	1.464 (0.047, 49.315)	0.821
Clinical TNM stage	II	reference	
	III	0.120 (0.003, 1.772)	0.170
PD-L1 CPS	<1	reference	
	≥1	2.855 (1.181, 3.079)	0.036

ECOG – Eastern Cooperative Oncology Group; TNM – tumor node metastasis; PD-L1 – programmed death-ligand 1; CPS – combined positive score; OR – odds ratio; 95% CI – 95% confidence interval.

Safety and follow-up

A summary of adverse events (AEs) is presented in Table 5. In the experimental group, the most prevalent AE was leukopenia, which was experienced by 23 out of 35 patients (65.7%). Other common AEs among patients included asthenia (62.9%), alopecia (60.0%), neutropenia (60.0%), rash (60.0%), and anemia (54.3%). The grade 3 or higher AEs included leukopenia in 2 cases (5.7%) and neutropenia in 12 cases (34.3%). One patient experienced a massive esophageal hemorrhage 3 weeks before surgery but was successfully treated and underwent successful surgery. Other AEs observed during neoadjuvant therapy included an increase in alanine aminotransferase (ALT), which occurred in 14 cases (40.0%), reactive cutaneous capillary endothelial proliferation (RCCEP), which occurred in 14 cases (40.0%), and increased aspartate aminotransferase, which occurred in 12 cases (34.3%). None of these caused any treatment suspensions, dose reductions or surgical delays, and the patients remained generally stable until the last follow-up. In the historical control group, alopecia was the most common AE, followed by asthenia, leukopenia, neutropenia, and rash, with hyperthyroidism being the least common. In addition, the 12-month DFS was 71.2%, and the 12-month OS rate was 94.4% in the experimental group (Fig. 3,4).

Discussion

This study prospectively evaluated the efficacy and safety of surgery after neoadjuvant camrelizumab combined with chemotherapy for the treatment of resectable ESCC. The study extended the neoadjuvant treatment regimen to 4 cycles, hoping to develop a more effective regimen to enhance the clinical outcomes in ESCC patients.

In the preoperative setting, chemotherapy combined with radiotherapy is the current standard neoadjuvant regimen, and it is being used as a combination partner of immunotherapy in many ongoing trials.[20,21] However, due to the toxic effects of radiotherapy, a less harmful regimen is being sought.[22] Thus, we were interested in exploring the response of ESCC to immunotherapy combined with chemotherapy. Indeed, in our study, neoadjuvant chemotherapy in conjunction with camrelizumab achieved a pCR rate of 51.4%, which was significantly higher than that of previously reported neoadjuvant immunotherapy combined with chemotherapy (22.2%, 25% and 46.2),[7,17,23] improving the pCR rate by 29.2%, 26.4% and 5.2%, respectively. The reason for this may be that the patients in the previous studies received only 2 or 3 cycles of neoadjuvant therapy, while our patients were treated with 4 cycles. In addition, 30 out of 35 surgical patients (85.7%) had degraded TNM staging after

Table 5. Adverse events

Adverse event, n (%)	Experimental group (n = 35)		Historical control group* (n = 23)	
	any grade	grade ≥3	any grade	grade ≥3
Leukopenia	23 (65.7)	2 (5.7)	14 (60.9)	2 (8.7)
Asthenia	22 (62.9)	0	15 (65.2)	0
Alopecia	21 (60.0)	0	19 (82.6)	0
Neutropenia	21 (60.0)	12 (34.3)	14 (60.9)	9 (39.1)
Rash	21 (60.0)	0	14 (60.9)	0
Anemia	19 (54.3)	0	13 (56.5)	0
Alanine aminotransferase increased	14 (40.0)	0	10 (43.5)	0
RCCEP	14 (40.0)	0	9 (39.1)	0
Aspartate aminotransferase increased	12 (34.3)	0	8 (34.8)	0
Hyperbilirubinemia	11 (31.4)	0	8 (34.8)	0
Thrombocytopenia	10 (28.6)	0	7 (30.4)	0
Decreased appetite	10 (28.6)	0	8 (34.8)	0
Vomiting	7 (20.0)	0	5 (21.7)	0
Oral mucositis	6 (17.1)	0	4 (17.4)	0
Diarrhea	5 (14.3)	0	3 (13.0)	0
Nausea	4 (11.4)	0	3 (13.0)	0
Constipation	4 (11.4)	0	3 (13.0)	0
Edema	3 (8.6)	0	2 (8.7)	0
Fever	3 (8.6)	0	2 (8.7)	0
Hyperthyroidism	1 (2.9)	0	1 (4.3)	0

RCCEP – reactive cutaneous capillary endothelial proliferation; * based on the results obtained by Yang et al.[17]

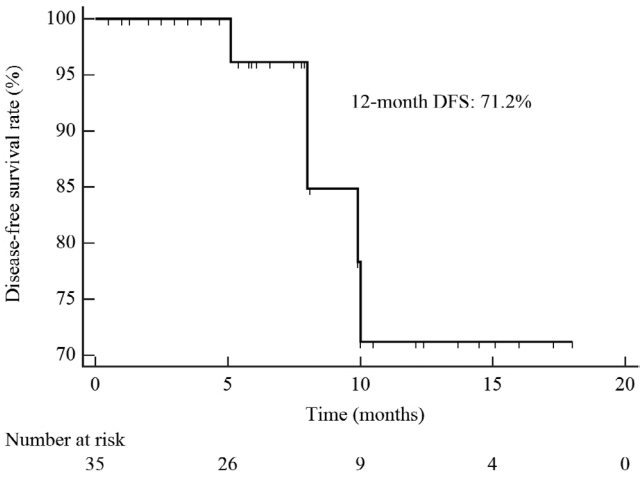

Fig. 3. Disease-free survival (DFS) curve of all patients who received surgery (n = 35)

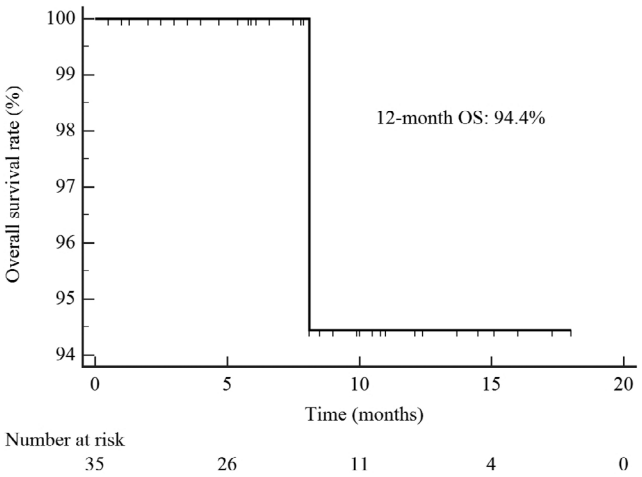

Fig. 4. Overall survival (OS) curve of all patients who received surgery (n = 35)

treatment, which is higher than that reported in the previous literature (65%).[17]

The findings of several important studies, including CROSS, NEOCRTEC5010 and the CheckMate 577 trial, have made neoadjuvant chemoradiotherapy combined with surgery a commonly accepted treatment option for resectable ESCC in Western countries.[8,10,24] The usage of neoadjuvant chemoradiotherapy is limited due to the added toxicity from chemotherapy and radiotherapy.[25,26] Reducing the dose to mitigate toxicity may reduce patient adherence, and neoadjuvant chemoradiotherapy can also lead to complications during surgery, such as tissue adhesion and swelling, and increase the risk of perioperative issues, such as radiation pneumonitis-induced respiratory failure, which may offset the intended survival benefits from neoadjuvant chemoradiotherapy.[27,28] Our study results indicate that leukopenia was the most frequently occurring AE, affecting 23 out of 35 patients. Other common AEs included asthenia, alopecia, neutropenia, rash, and anemia. We also identified grade 3 or higher AEs, including leukopenia in 2 cases

and neutropenia in 12 cases. Regarding postoperative complications, our study found a 2.9% incidence of anastomotic leakage, which is lower than what was previously reported in the CROSS study (22%). It should be noted that the study reports successful treatment and surgery of 1 patient who experienced massive esophageal hemorrhage 3 weeks prior to surgery. We detected increased levels of alanine aminotransferase in 14 cases, RCCEP in 14 cases and increased levels of aspartate aminotransferase in 12 cases, but none of these resulted in treatment suspensions, dose reductions or surgical delays.

Previous research has shown that several clinical biomarkers, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR), have moderate predictive value for prognosis. However, their potential for predicting the efficacy of immunotherapy remains rarely reported.[29,30] In recent years, the importance of PD-L1 expression level has been a popular topic in immunotherapy. However, earlier clinical trial results indicate that immunotherapy combined with chemotherapy is beneficial in the entire population, including those with negative PD-L1 expression, which led to PD-L1 detection being non-essential.[31,32] Interestingly, our exploratory analysis showed that patients with higher PD-L1 expression were more likely to benefit from neoadjuvant therapies; thus, the PD-L1 expression seems to be a predictive factor for pCR after neoadjuvant immunotherapy. In addition, patients aged >65 years achieved a lower pCR, which may be attributed to the physiologic decline in the functions of major organs in older patients.[33] The guiding value of age and PD-L1 expression level in immunotherapy should be recognized and is worthy of further exploration in future large sample studies.

Limitations

There are 2 limitations to this study. First, the sample size was small, implying that a larger cohort is necessary to further validate these findings. Second, owing to the short duration of follow-up, median DFS and OS were not reported, but follow-up is still in progress.

Conclusions

In conclusion, the results of this study suggest that the extension of the treatment cycle to 4 cycles of neoadjuvant camrelizumab combined with chemotherapy may offer a promising treatment option for patients with resectable ESCC. Further large-sample studies are needed to confirm these results.

Data availability statement

The data from this study are available from the corresponding author upon reasonable request.

Supplementary data

The supplementary materials are available at https://doi.org/10.5281/zenodo.8199073. The package contains the following files:

Supplementary Table 1. The results of Box–Tidwell test.

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