

Does Consolidation Chemotherapy improve Patient Survival in Locally Advanced Non-Small-Cell Lung Cancer?

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ABSTRACT

The role of consolidation chemotherapy is being investigated due to inconclusive outcomes, ascribed to high rates of recurrence and mortality with standard concurrent chemoradiotherapy (CRT) in patients with unresectable locally advanced non-small-cell lung cancer (LA-NSCLC). We evaluated the impact of consolidation chemotherapy on the survival of patients with LA-NSCLC at our single medical centre. In total, 136 patients with unresected LA-NSCLC were evaluated to identify and compare the factors influencing survival rates. The median overall survival (OS) was 27 and 23.6 months and median progression-free survival (PFS) was 12.3 and 12.8 months in the CRT and consolidation treatment groups ($p=0.840$ and 0.808), respectively. Consolidation chemotherapy after concurrent CRT experiences has neither OS nor PFS survival benefit, compared with concurrent CRT alone. Thus, our study did not support favourable consolidation chemotherapy in patients with LA-NSCLC.

Keywords: Locally advanced non-small cell lung cancer, Consolidation chemotherapy, Concurrent chemoradiotherapy, Overall survival, Progression-free survival

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths worldwide and accounts for 18.4% of total cancer mortalities.¹ According to the GLOBOCAN survey involving 185 countries, the global burden of the disease was ~ 2.1 million new lung cancers and 1.76 million deaths.¹

Non-small cell lung cancer (NSCLC) represents about 80-85% of all newly diagnosed lung cancer cases.² NSCLC is a lethal heterogeneous condition with a five-year survival rate ranging from 50% in pathological stage I to 2% in stage IV.^{2,3} Approximately one-third of all NSCLC patients are diagnosed with stage III locally advanced NSCLC disease, and only a minority of these cases are considered operable.⁴ While recent advances in

diagnostic and therapeutic agents have improved the management of the advanced disease, limited progress has been achieved in the diagnosis and treatment of early and locally advanced NSCLC (LA-NSCLC) disease stages.⁵

The management options for patients with stage III NSCLC include a combined modality therapy approach, such as combinations of surgery, chemotherapy and radiotherapy. Chemotherapy can be administered to patients before radiation (defined as sequential) or during radiation (defined as concurrent). Treatment can be applied as induction-concurrent (chemotherapy before and during radiation) or concurrent consolidation (chemotherapy during and after radiotherapy).⁶

The standard treatment for patients with grade III LA-NSCLC is platinum-based chemotherapy followed by active surveillance with CRT, which provides improved overall survival (OS), as compared with sequential CRT or radiotherapy alone.⁷ A meta-analysis that included 19 randomised trials in 2010 showed an 8% reduction in mortality with CRT, as compared with that with single modality radiotherapy and a 13% reduction compared with sequential CRT.⁸ However, the outcome of CRT in patients with grade III NSCLC is still not encouraging, with 5-year OS rates ranging between 15%-25%.⁹ The addition of consolidation chemotherapy has emerged as a potential treatment strategy, and many studies have focused on investigating the feasibility and effectiveness of this treatment following concurrent CRT administration in terms of possible improvements in PFS and OS.^{4,10} However, the efficacy of consolidation chemotherapy after concurrent CRT in patients with locally advanced NSCLC remains controversial. Given the lack of a significant benefit of survival for LA-NSCLC patients in a randomised phase III trial¹¹ and observed pooled analysis from 45 studies¹², the definitive role of consolidation chemotherapy is unknown.

We aimed to evaluate the efficacy of platinum-based consolidation chemotherapy following concurrent CRT treatment and compare outcomes with concurrent CRT alone therapy in terms of their effects on PFS and OS in patients with locally advanced NSCLC.

MATERIALS AND METHODS

Patient Selection

This research was a single-centre retrospective study and was carried out from October 2009–March 2018 as a cohort study at our hospital. A total of 136 patients diagnosed with unresectable locally advanced NSCLC who had received concurrent CRT with or without consolidation chemotherapy were included in the study. The participants were categorised into two groups based on whether they received consolidation chemotherapy or concurrent CRT.

All patients were histologically or cytologically proven to have NSCLC, diagnosed as stage III in

accordance with the staging system of the American Joint Committee on Cancer in 2009 and Tumour Nodes Metastasis (TNM) classification.¹³ The diagnosis of the unresectable stage III LA-NSCLC disease was confirmed in most cases via up chest radiography, abdominal and thoracic computed tomography (CT) scans, brain magnetic resonance imaging to eradicate the presence of metastasis, bronchoscopy, endobronchial ultrasonography and FDG-positron emission tomography of the lungs. Clinical and demographic data of patients, including age, gender, smoking history, physical performance status, types of chemotherapy combination, dose reduction, the date of progression and last outpatient control or the date of exitus, were obtained from the hospital records.

Study Design

The patients were categorised into two groups and evaluated according to the administered treatment schedule. The first group was the consolidation group who received consolidation chemotherapy after concurrent CRT, and the second group comprised those who received concurrent CRT alone. In the consolidation group, in addition to prior CRT treatment, carboplatin plus paclitaxel or cisplatin plus etoposide were given as two cycles every 21 days. The records of the follow-up evaluations of all patients were used to obtain physical examination findings, complete blood cell counts (CBC), serum biochemistry, tumour markers, thoracic and abdominal CT scans and positron emission tomography for the suspicion of metastasis during 2 months after treatment.

The clinical and imaging examinations were performed every 3 months for the first year, and every 6 months in the following years. During the concurrent CRT period, CBC and serum biochemistry examinations were performed once a week. First response assessment was classified in three groups: partial response, stable disease or progressive disease according to Response Evaluation Criteria in Solid Tumors (RECIST version 1.1)¹⁴, as follows: Partial response (PR) was defined as at least 30% reduction from baseline in the longest diameters of target lesions. Progressive disease (PD) was defined as at least a 20% increase from baseline in

the sum of longest diameters of target lesions or the appearance of one or more new lesions. Stable disease was defined as neither adequate lesion shrinkage to qualify for PR nor sufficient increase to qualify for PD. Relapses were recorded as local relapse or distant metastasis, and determined, as follows: Local relapse was defined as primary tumour recurrence or regional recurrence. Distant metastases were characterised by contralateral lung metastatic lymph nodes in the neck or axilla or metastasis to any other organ. If local relapse and distant metastasis were detected simultaneously, it was named 'Local and Distant Relapse', as shown Table 1. Disease progression was ascertained based on cytohistological or radiological examinations. Adverse effects were recorded via the electronic health information system of the hospital.

Statistical Analysis

The statistical analysis was performed using the SPSS software, version 18.0 (SPSS Inc. Chicago, IL, USA). Descriptive statistics were reported as percentages and medians. The demographic and clinical characteristics of patients were presented as medians and frequencies. OS was described as the time from diagnosis until death or last follow-up. PFS was described as the time from treatment initiation to disease progression or death. Progression was defined as local recurrence and/or distant metastasis. The groups were compared in terms of PFS and OS. Besides, the groups were compared according to age, gender, smoking duration, presence of dose reduction, response assessment, chemoregimens with concurrent radiotherapy and types of recurrence with local or distant metastasis. Categorical variables were analysed using chi-square or Fisher's exact test. Survival curves were obtained, and survival rates were determined using the Kaplan–Meier method, and comparisons were made with the log-rank test. Significant factors were identified in univariate analyses and were entered into a backward selection Cox regression model to determine independent predictors of survival. Univariate and multivariate analyses using a Cox proportional hazards (HZs) model was performed to assess potential prognostic factors for OS and PFS. A p-value of 0.05 or lower (p value < 0.05) was considered statistically significant.

RESULTS

A total of 136 patients with grade III NSCLC were included retrospectively in the study. The median age of the patients was 63 years (range: 42-82 years) and mostly male ($n=120$, 88.2%). In pathological examinations, the patients were diagnosed with various types of lung cancer, including squamous cell cancer (SCC), adenocarcinoma, not otherwise specified and large cell carcinoma (63.2%, 30.9%, 5.1% and 0.7%, respectively). Precisely, 74 (54.4%) patients were in stage IIIA and 62 (45.6%) patients in stage IIIB. The Eastern Cooperative Oncology Group performance status (ECOG PS) was utilised to determine functional status; that is, the patients' ability to tolerate therapy under the severe disease condition. We found that the vast majority of patients' positive responses (95.6%). Their mean smoking status was 41.2 packets/year.

Among the 136 patients, 77 patients (56.6%) received consolidation chemotherapy after concurrent CRT, while 59 (43.4%) patients were treated with concurrent CRT alone. A combination of treatments, consisting of cisplatin plus etoposide or carboplatin plus paclitaxel were used in the majority of participants, as the chemotherapy regimen ($n=77$) and 16 of the 77 cases were administered with cisplatin as a single agent with concurrent CRT. All patients were administered curative thoracic radiotherapy with a minimum dose of 60 Gy radiation. For the concurrent CRT regimen, 68 (50%) of the patients were treated with carboplatin plus paclitaxel, 50 (36.8%) patients were administered cisplatin plus etoposide and 18 (13.2%) patients received other platinum-containing regimens, including weekly cisplatin, cisplatin plus vinorelbine and cisplatin plus pemetrexed. Dose reduction was performed in 18 (13.2%) patients due to adverse effects, including mucositis, renal toxicity, thrombocytopenia and neutropenia. No significant difference was detected between groups in the sense of dose reduction ($p=0.139$). After concurrent CRT, the consolidation group ($n=77$) received two cycles of cisplatin- or carboplatin-based consolidation chemotherapy. The assessment of post-treatment responses showed local relapse in 42 patients (30.8%), distant metastasis in 16 patients (11.7%) and both in 9 patients (6.6%). Metastasis localisations were as follows: brain (8.1%), bone (8%),

Table 1. Demographic and clinical data of locally advanced non-small-cell lung cancer patients

		C-CRT	CC-CRT	p-value
Gender	Male	52 (88.1%)	68 (88.3%)	0.975
	Female	7 (11.9%)	9 (11.7%)	
Age (median)		71.1	66.4	0.496
Smoking Status	≤ 40 pc/y	25 (45.5%)	30 (39%)	0.285
	> 40 pc/y	30 (54.6%)	47 (61%)	0.110
ECOG PS	≤ 1	56 (94.9%)	76 (98.7%)	
Stage	III a	40 (69.0%)	34 (43.6%)	0.003*
	III b	18 (31.0%)	44 (56.4%)	
Histological type	SCC	41 (69.5%)	45 (55.4%)	0.298
	Non-SCC	18 (30.5%)	32 (41.6%)	
Dose reduction	Yes	4 (6.9%)	14 (18.2%)	0.056
	No	54 (93.1%)	63 (81.8%)	
Chemotherapy	Cisplatin-based	34 (57.6%)	26 (33.8%)	0.005*
	Carboplatin-based	25 (42.4%)	51 (66.2%)	
Response	PR at least	28 (47.5%)	45 (58.4%)	0.394
	Non-PR	21 (35.6%)	27 (35.1%)	
Relapse	Local relapse	22 (73.3%)	20 (40%)	0.009*
	Distant metastasis	6 (20%)	10 (20%)	
	Local and distant	1 (3.1%)	8 (16%)	

C-CRT= Concurrent chemoradiotherapy, CC-CRT= Consolidation after concurrent chemoradiotherapy, pc/y= packet/year, ECOG PS= Eastern Cooperative Oncology Group Performance Status, SCC= Squamous cell carcinoma, CR= Complete remission, PR= Partial remission, *p< 0.05

pleura (3.6%), liver (2.2%) and adrenal gland (2.2%).

Patient characteristics are shown in Table 1. No significant differences were found between the concurrent CRT only group and the consolidation treatment group in terms of gender, age, smoking status, histological subtype and ECOG PS performance status ($p > 0.05$ for all). Carboplatin-based chemotherapy was used more frequently than cisplatin-based chemotherapy in the consolidation treatment group ($p = 0.005$). Before the treatment, 44 patients were in stage IIIB in the consolidation group, while this number was 18 in the CRT only group ($p = 0.004$).

Partial and complete response, named at least PR due to less of CR, only two patients, in Table 1, was observed in 28 patients (47.5%) in the CRT group and in 45 patients (58.4%) in the consolidation chemotherapy group ($p < 0.001$). In the CRT group, 22 patients (73.3%) had a local relapse, 6

patients (20%) had distant metastasis, while 1 patient (3.1%) had both local and distant metastasis. Post-treatment responses in the consolidation group revealed local relapse in 20 patients (40%), distant metastasis in 10 patients (20%) and both in 8 patients (16%) ($p = 0.009$).

The median OS and PFS for all patients were 25.2 months and 12.8 months, respectively. The median OS was 27 months (range: 17.6-36.3) in the CRT group and 23.6 months (range: 18.2-29) in the consolidation treatment group ($p = 0.840$). Median PFS was 12.3 months (range: 7.7-16.9) in the CRT group and 12.8 months (range: 9.7-16) in the consolidation chemotherapy group ($p = 0.808$). Therefore, no significant differences were found between the two groups in terms of PFS or OS (Figures 1 and 2).

The univariate analysis of prognostic factors for OS and PFS are shown in Table 2. We utilised this analysis to identify that having < 40 packets/

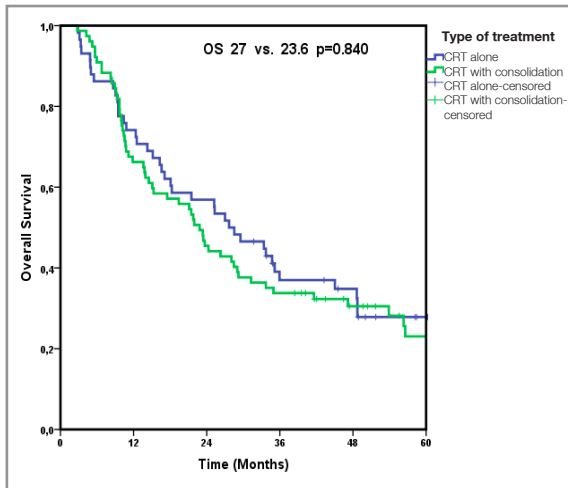


Figure 1. Kaplan–Meier curves of OS

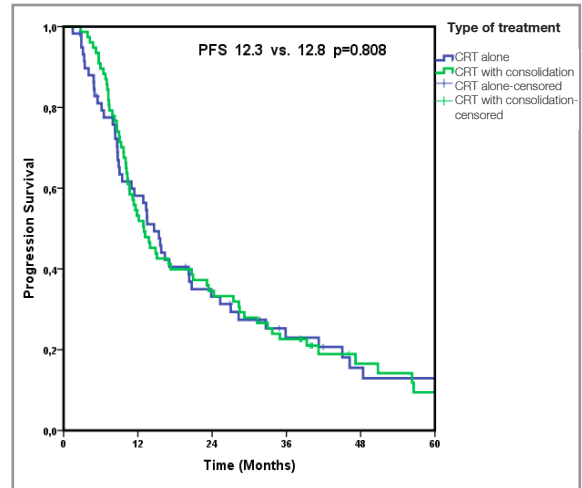


Figure 2. Kaplan–Meier curves of PFS

year of smoking ($p = 0.025$) and partial remission ($p < 0.001$) were significant prognostic factors for PFS and OS. Following the univariate analyses, smoking status and treatment response were evaluated in multivariate analyses, which showed that smoking of < 40 packets/year and positive treatment response were two potential prognostic factors for survival. The mortality risk ratio of patients without PR was 2.1 (Hazard ratio range: 1.3-3.5, $p = 0.001$). Also, patients with PR (at least) were found to have statistically significant prolonged PFS (HR: 1.6, range: 1.0-2.6, $p = 0.038$). Smoking < 40 packets/years was also associated with longer PFS (HR: 1.7, range: 1.0-2.8, $p = 0.028$). However, when the smoking status was evaluated in multivariate analysis for OS, we found no significant relationship (Table 3).

In consideration of adverse side effects, nausea ($n = 104$, 76.4%), vomiting ($n = 32$, 23.5%), fatigue ($n = 110$, 80.8%), mucositis ($n = 39$, 28.6%), stomatitis ($n = 26$, 19.1%), neuropathy ($n = 37$, 27.2%), nephrotoxicity ($n = 7$, 5.1%), hepatotoxicity ($n = 8$, 5.8%), neutropenia ($n = 53$, 38.9%), thrombocytopenia ($n = 13$, 9.5%) and anaemia ($n = 34$, 25%) were seen. Due to a lack of side effects timing of the patients, comparable analyses were not performed between the consolidation and the CRT alone groups. However, side effects were evaluated due to carboplatin and cisplatin-based chemotherapy. As shown in Table 4, significant differences were detected for nausea, vomiting, fatigue, mucositis, stomatitis

and neuropathy in carboplatin and cisplatin-based chemotherapy groups regardless of consolidation. We could not perform analysis regarding toxicity grade due to prolonged insufficient recorded dates on patients' files.

DISCUSSION

The current study aimed to assess the impact of consolidation chemotherapy on PFS and OS in patients with LA-NSCLC, known to have a wide range of clinical presentations, rendering the disease rather heterogeneous.¹⁵ The standard treatment for patients with inoperable stage III LA-NSCLC is concurrent chemoradiotherapy, which appears to enable local control of recurrence, decrease the development of distant metastasis and prolong survival.^{11,16} However, LA-NSCLC disease has a poor prognosis, and median survival times are only 12-23.2 months.⁹

Concurrent CRT plays a role as a radiosensitiser for the primary tumour area; however, due to dose management to avoid compromising disease control, the dosage might be insufficient for therapeutic performance for effective disease treatment.¹⁷ Therefore, it has been reported consistently that consolidation chemotherapy regimens might have different effects on the systemic disease, depending on several factors, including the number of cycles administered, chemotherapy regimens and

Table 2. Results of the univariate analyses of prognostic factors for OS and PFS

		Month (OS)	p-value (OS)	Month (PFS)	p-value (PFS)
Gender	Male	24.2 (18.8- 28.7)	0.42	12.9 (8.8- 17.0)	0.87
	Female	26.2 (19.8- 30.6)		11.8 (7.1- 16.4)	
Age	≤ 60 years	21.4 (13.6- 29.2)	0.65	11.3 (9.9- 12.7)	0.33
	> 60 years	29 (16.7- 41.2)		13.9 (6.9- 20.9)	
Smoking Status	≤ 40 pc/y	27 (18.6-35.4)	0.28	15.1 (1.9- 28.4)	0.025*
	> 40 pc/y	21.9 (11.7- 32.1)		11.8 (8- 15.6)	
Stage	III a	27.6 (20- 35.2)	0.85	15.4 (10.1-20.6)	0.75
	III b	23.6 (14.5- 32.8)		11.3 (8.2-14.4)	
Location	Right hemithorax	25.2 (18- 32.3)	0.73	14.6 (7.7- 21.5)	0.98
	Left hemithorax	25.2 (13.9- 36.6)		11.8 (9.5- 14)	
Hystologic types	SCC	23.3 (16-30.7)	0.80	10.9 (6.9- 15)	0.72
	Non- SCC	27.6 (17.2- 38)		16.3 (9.7- 22.9)	
Chemotherapy	Cisplatin based	27.6 (13.3- 42.9)	0.83	12.3 (6.4- 18.3)	0.40
	Carboplatin based	27 (11.2- 42.7)		14.6 (7.9- 21.3)	
Consolidation CT	Cisplatin based	29 (17.3-40.6)	0.43	19.9 (3.8- 36)	0.33
	Carboplatin based	21.9 (12- 31.8)		11.8 (8.6- 15)	
Response	PR	48.6 (22.2- 74.9)	0.003*	26.1 (11.7-40.5)	<0.001*
	Non- PR	14.4 (10.2- 18.6)		9 (7- 11)	
Dose reduction	Yes	21.4 (11- 31.8)	0.85	10.6 (6.9- 15)	0.24
	No	26.2 (20.3- 32.1)		12.9 (8.8- 17.1)	

OS= Overall survival, PFS= Progression-free survival, SCC= Squamous cell carcinoma, CT= Chemotherapy, PR= Partial remission (response), pc/y= packet/years, *p-value < 0.05

pre-consolidation therapies.¹⁶⁻¹⁸ However, currently, study outcomes with added consolidation CRT, seem to be inconclusive and somewhat controversial in many aspects. Hanna et al.¹¹ demonstrated that there were no differences between PFS and OS in a randomised phase III clinical trial with 73 patients who were assigned to the docetaxel-consolidation group (3 cycles) and 74 patients who were enrolled as an observational group (both after concurrent CRT with cisplatin etoposide). Consistent with our results, we did not find any prolonged survival with a similar number of patient participants and we performed two cycles of consolidation therapy with various regimens in our study. Similarly, a multinational, randomised phase III study, involving 419 patients with grade III NSCLC conducted by Park et al.¹⁹ showed that consolidation therapy with three cycles of docetaxel-cisplatin failed to improve PFS in comparison with the observation group. These outcomes are again consistent with

our findings. Further, Jalal and colleagues²⁰, in their phase III trial for LA-NSCLC with or without consolidation therapy after CRT, revealed that additional docetaxel therapy provided no benefit for survival, but rather, rendered higher rates of toxicity and hospitalisation. A pooled analysis of the literature, including 34 phase II studies and 7 phase III studies conducted by Tsujino et al.¹² demonstrated that consolidation chemotherapy after CRT failed to yield a favourable survival outcome or risk reduction in the mortality of patients with LA-NSCLC.

In our study, we found differences between our two groups for the stage, choice of platin-based treatment and type of relapse, while the outcomes of the OS and PFS were similar in both groups. We noticed conflicting results available in the literature: Mutlu et al.²¹ showed in 74 inoperable patients with locally advanced NSCLC that consolidation treatment had better outcomes concerning OS and

Table 3. Results of the multivariate analyses of prognostic factors for OS and PFS

	PFS HR (95% CI)	p-value (PFS)	OS HR (95% CI)	p-value (OS)
Smoking time				
≤ 40 pc/y	Reference		Reference	
> 40 pc/y	1.7 (1-2.8)	0.028*	1.1 (0.7-1.8)	0.411
Response				
PR (at least)	Reference		Reference	
Non-PR	1.6 (1-2.6)	0.038*	2.1 (1.3-3.5)	0.001*

OS= Overall survival; PFS= Progression-free survival; HR= Hazard ratio; CI= Confidence interval; PR= Partial response

PFS, compared with induction chemotherapy, followed by CRT or CRT alone. In their study, all the patients were in stage IIIB with a TNM classification of T4N2M0, which might explain the results, as these patients might need more systemic chemotherapy to eradicate micrometastases and circulating tumour cells; thus, this could possibly cause an alteration in the efficacy of additional therapy.

Wang et al.⁴, in a meta-analysis, including five separate studies, reported that the treatment of LANSCLC with CRT, followed by consolidation therapy, improved OS, but not PFS. In another study, Liu et al.¹⁸ demonstrated in a retrospective study, with 113 patients' inclusion who received consolidation therapy for at least two cycles and 90 patients who received CRT alone, that consolida-

Table 4. Differences in the side effects of platin-based chemotherapies regardless of consolidation

Side effect		Cisplatin-based (%)	Carboplatin-based (%)	p-value (*<0.05)
Nausea	Yes	54 (91.5)	50 (64.9)	< 0.001*
	No	5 (8.5)	27 (35.1)	
Vomiting	Yes	20 (33.8)	12 (15.5)	0.012*
	No	39 (66.2)	65 (84.5)	
Fatigue	Yes	56 (95)	53 (68.9)	< 0.001*
	No	3 (5)	24 (31.1)	
Mucositis	Yes	26 (44)	13 (16.8)	0.001*
	No	33 (56)	64 (83.2)	
Stomatitis	Yes	17 (28.8)	9 (11.6)	0.011*
	No	42 (71.2)	68 (88.4)	
Neuropathy	Yes	6 (10.1)	31 (40.2)	< 0.001*
	No	53 (89.9)	46 (59.8)	
Nephrotoxicity	Yes	3 (5)	4 (5.1)	0.166
	No	56 (95)	73 (94.9)	
Hepatotoxicity	Yes	3 (5)	5 (6.9)	0.566
	No	56 (95)	72 (93.1)	
Neutropenia	Yes	23 (38.9)	30 (38.9)	0.569
	No	36 (61.1)	47 (61.1)	
Thrombocytopenia	Yes	7 (11.8)	6 (7.7)	0.304
	No	52 (88.2)	71 (92.3)	
Anaemia	Yes	16 (27.1)	18 (23.3)	0.381
	No	43 (72.9)	59 (76.7)	

tion treatment had significantly better survival than CRT alone (median OS: 27 months vs. 16 months; 5-year OS: 30.4% vs. 22.5%, $p=0.012$) without increased toxicity. Moreover, they showed better survival advantages with consolidation chemotherapy after concurrent CRT mostly in the following groups of patients: those aged < 60 years, males, those with non-squamous histology, patients with stage IIIB disease, those that showed treatment response and recipients of radiotherapy dose ≥ 60 Gy.¹⁸

Prognostic factors are critical in the evaluation of disease progression and treatment modalities. The widely accepted prognostic factors for LA-NSCLC include female gender, stage IIIA, weight loss and good performance status.^{18,22} In our study, we found that treatment response and smoking status are significant prognostic factors for PFS and OS. We revealed that patients with PR had 1.6 times longer PFS and 2.1 times longer OS than patients without PR. Our results support the view of Jeremic and colleagues²³, who suggested that patients with complete or PR were more likely to benefit from consolidation therapy. We also observed that smoking cigarettes < 40 packets/year associated with 1.7 times longer PFS than smoking > 40 packets/year. The PFS disadvantage of high smoking history, as a prognostic factor, might be relevant co-morbidities.²⁴ However, any data of comorbidity was recorded.

Further, our study found a difference between the two groups in terms of the cancer stage. More stage IIIA patients were identified in the CRT group, whereas stage IIIB was more common in the consolidation group. Thus, we expected this observation to make a difference between the groups in univariate analysis; however, the CRT group might not have been able to display prolonged survival due to the absence of consolidation chemotherapy. Tsujino et al.¹² aimed to evaluate whether consolidation chemotherapy, after concurrent CRT, is beneficial based on the same goal as our group. They published a pooled analysis from the literature, and, interestingly, found no difference between the consolidation group and the CRT group in terms of stage III and IIIB disease, presenting < 33% of the ratio in stage IIIA group having shorter OS. Contrary to our study, which failed to show an appreci-

able difference, possibly due to the smaller number of study participants.

Although the optimal chemoregimen in the treatment of LA-NSCLC could not be selected, platinum-based chemotherapies are preferred to radiosensitising agents.¹⁵ According to our literature review, and in our study in which cisplatin-based and carboplatin-based chemotherapies were chosen, carboplatin-based treatment, in particular, was more noticeable in our consolidation group than the concurrent CRT group. Ezer et al.²⁵ showed that carboplatin-based CRT displayed a parallel survival association with lower rates of toxicities. However, we did not notice any survival difference in our carboplatin-based group, which is in agreement with the indicated study.

Our present study does not preclude limitations. First, because of the nature of the retrospective study design, our analyses do not represent homogeneous data tending to no constant treatment choice at the centre. This situation could obstruct the achievement of more meaningful results. Second, our study included heterogeneous consolidation regimens, unequal treatment arms and heterogeneous radiotherapy dosages (despite defining a threshold of at least 60 Gy), likely to affect our conclusions. Third, we examined patients from a single centre with similar ethnicity (Turkish population). Thus, patient characteristics, including ethnicity, might have played a significant role in survival and response rate to chemotherapy in lung cancer.²⁶

Conclusion

In conclusion, we found no significant differences between the CRT only group and the consolidation treatment group regarding PFS and OS. Additionally, our results demonstrated that patients with grade III NSCLC treated by consolidation chemotherapy after prior concurrent CRT experiences have no survival benefit, compared with those treated with concurrent CRT alone. Further, we showed that smoking status and treatment response were prognostic factors for PFS and OS. Therefore, clinical studies with novel treatment approaches, including molecular-targeted utilisation of targeted agents and innovative immunotherapy

strategies are necessary to establish the feasibility of consolidation chemotherapy regimens.

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