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Original Research Article

A comparative study on tumour response, intrathoracic symptom palliation and toxicities in locally advanced inoperable non-small cell lung cancer patients receiving palliative chemoradiation versus radiation alone

Ruby Panmei[1]*, Yumkhaibam Sobita Devi[1], Angom Ronibala Devi[1], Dorafiona Swer[1], Ningthoujam Dinita Devi[2], Rahul Mahawar[2]

[1]Department of Radiation Oncology, Regional Institute of Medical Sciences, Imphal, Manipur India
[2]Department of Radiation Oncology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India

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***Correspondence:**
Dr. Ruby Panmei,
E-mail: rubypanmei@gmail.com

ABSTRACT

Background: Locally advanced unresectable non-small cell lung cancer (LA-NSCLC) is a key focus in research, as it presents significant treatment challenges, with low survival rates despite progress in radiotherapy and systemic therapies. This study compares two palliative regimen for LA-NSCLC, one with radiation alone the other arm as concurrent chemoradiation therapy (CCRT) with nab-paclitaxel.
Methods: A Randomised Controlled Trial was conducted in the Department of Radiation Oncology, Regional Institute of Medical Sciences, Imphal from July 2022 to June 2024. Sample size of 96 was calculated. In the Control Arm (Arm A), patients were treated with radiation alone at the dose of 36 Gy/12# and in the Study Arm (Arm B), CCRT was given at 40 Gy/20 with nab-paclitaxel given as a weekly dose. The primary endpoint is to see the tumour response, intrathoracic symptom palliation and treatment toxicities between the two arms. Secondary endpoints include progression-free survival (PFS).
Results: Our study has a better overall response rate in Arm B compared to Arm A and the most effectively palliated symptoms in our study were chest pain and shortness of breath. Arm B exhibited more pronounced acute and late radiation toxicities which were manageable. The median PFS was 8 months in Arm A and 13 months in Arm B.
Conclusions: Overall response rate after completion of treatment was higher in palliative concurrent chemoradiation group as compared to palliative radiation therapy group, but in totality, the two palliative lung cancer treatment regimens were almost equal in efficacy in terms of intrathoracic symptom palliation and toxicity

Keywords: Unresectable non-small cell lung cancer, Palliative chemoradiation, Nab-paclitaxel, intrathoracic symptom palliation

INTRODUCTION

Globally, lung cancer was the most diagnosed cancer worldwide, with 2.5 million new cases (12.4% of all cancers), followed by breast cancer (11.6%) (GLOBOCAN 2022). It was also the leading cause of cancer death, responsible for 1.8 million deaths (18.7%). Lung and breast cancer were the most common cancers in men and women, respectively. In India, lung cancer accounted for 5.8% of new cases and 8.2% of cancer-related deaths.[1] Histopathologically, lung cancer can be categorized as non-small cell lung cancer (NSCLC) and

small cell lung cancer (SCLC)[2] non-small cell lung cancers (NSCLC) account for 85%–90% of lung cancers while small-cell lung cancer (SCLC) has been decreasing in frequency in many countries over the last two decades.[3]

NSCLC is staged according to TNM staging based on tumour size, involvement of regional lymph nodes and whether it has spread outside the lung. Stage I and II NSCLC are early stage, stage III is loco-regionally advanced and stage IV is metastatic NSCLC.[4] To date, a majority of lung cancer cases are diagnosed in symptomatic individuals with the most common symptoms being cough, fatigue, dyspnoea, chest pain, weight loss and hemoptysis.[5]

NSCLC treatment typically involves surgery, radiotherapy, chemotherapy, immunotherapy or molecularly targeted therapy, either alone or in combination. Surgical resection is recommended for medically fit patients with early-stage NSCLC (stages I, II and IIIA), especially when N2 lymph node involvement is found during surgery.[6] Palliative care is used for stage IIIB and IV NSCLC. Stage IIIB is not curable and stage IV is managed to extend survival, control symptoms and improve quality of life. Treatment options include chemotherapy, radiotherapy and supportive care.[7]

Concurrent chemoradiotherapy (CCRT) has been considered to be the standard of care for locally advanced unresectable stage III non-small-cell lung cancer (LA-NSCLC).[8] A randomized phase III trial results of the Trans-Tasman radiation oncology group 11.03 done by Lehman M et al, on palliative radiation therapy versus concurrent chemotherapy and palliative radiation therapy, in patients of NSCLC who were not suitable for radical chemoradiation, received palliative radiation therapy (PRT36/12) on one arm and concurrent chemotherapy and PRT (C-PRT40/20) on the other arm given concurrently with cisplatin and vinorelbine.[9]

The study shows that there was no difference between the arms in overall quality of life, toxicity and progression-free survival between baseline and 6 weeks post-treatment. A non-statistically significant 3 months improvement in median survival favoured C-PRT(40/20). However, chemotherapy added to PRT(40/20) did not provide superior symptomatic relief. This study demonstrates that both treatments effectively alleviated the individual symptoms, with no significant difference between the trial groups.

Nab-PTX is a paclitaxel formulation where paclitaxel nanoparticles are bound to human serum albumin. A prior study showed that nab-PTX increased intra-tumoral paclitaxel levels and antitumor activity more than Cremophor-based paclitaxel at the same dose.[10]

The updated phase I/II study results show that concurrent chemoradiation with carboplatin, nab-paclitaxel (nab-PTX) and radiotherapy is safe, feasible and offers long-term survival benefits for patients with locally advanced NSCLC.[11] Nab-PTX as first-line therapy for advanced NSCLC improved overall response rate and reduced neuropathy compared to solvent-based paclitaxel, meeting the primary endpoint.[10]

However, there is less clinical study on palliative chemoradiation with nab-paclitaxel till date for symptom management and also to improve the quality of life. In view of limited data, this study was taken up to evaluate the tumour response, intrathoracic symptom palliation and toxicities in patients with inoperable NSCLC using intravenous nab-paclitaxel and radiation versus radiation therapy alone.

METHODS

A Randomised Controlled Trial was conducted in the Department of Radiation Oncology, Regional Institute of Medical Sciences, Imphal from July 2022 to June 2024, with prior approval from the Institution's Research Ethics Board (REB). Our study population includes patients who were histopathologically/cytologically confirmed cases of locally advanced inoperable NSCLC who reported to our department. The total sample size was calculated at 96, with 48 in each arm.

Inclusion criteria

inclusion criteria were locally advanced inoperable NSCLC (Stage IIIB, IIIC), above 30 years and below 70 years, Karnofsky performance status (KPS)≥60%, adequate haematological counts.

Exclusion criteria

Exclusion criteria Exclusion criteria included patients with prior anti-cancer treatment, second malignancies, psychosis, liver cirrhosis, massive pleural or pericardial effusion, positive contralateral supraclavicular lymph nodes and metastatic lesions. Patients were allocated to Control arm (arm-A) and study arm (arm-B) by using simple randomization method (Lottery method).

All the histopathologically confirmed patients were subjected for complete history, thorough general physical examination, complete blood count, blood chemistry including LFT, KFT, SE and blood sugar, urine routine examination, Echocardiogram, chest X-ray (PA and lateral view), ultrasound whole abdomen and contrast enhanced computed tomography (CECT) scan of thorax.

In Arm A, patients were treated with Theratron 780 C telecobalt machine in two-dimensional external beam radiation therapy using Source to Skin Distance (SSD) of 80cm at the dose of 36 Gy/12 and in Arm B, CCRT was given at 40 Gy/20 with telecobalt machine with nab-paclitaxel 60 mg/m2 over 60 mins every weekly preferably on the 1st day of the week beginning from the initiation of radiation therapy (day 1, 8, 15 and 22). The planned target

volume for both the Arms included primary disease and lymphatic metastatic disease with a margin of 2 cm. Ipsilateral hilum in N2 and bilateral hilum in N3 were also included. Radiation was delivered by two opposing antero-posterior and postero-anterior fields. The biologically effective dose (BED) for both the regimen are almost similar. Organ at risk including spinal cord were not considered for both the cases BED is less than the tolerance doses.

Patients were assessed weekly through physical exams to monitor treatment toxicity, with complete blood counts and biochemical tests (LFT, KFT) conducted each week. Treatment was paused if Hb%<10 gm/dl, TLC<4000/cu-mm or platelets <1 lakh/cu-mm. Blood transfusions or G-CSF/GM-CSF were administered based on blood parameter changes.

The tumour response (both primary and nodal) was assessed by response evaluation criteria in solid tumours (RECIST Criteria) after six weeks of completion of treatment. Intrathoracic symptoms were assessed before starting the treatment (Pre-treatment intrathoracic symptoms) and at 1st and 3rd months (post-treatment intrathoracic symptoms) after completion of treatment. Intrathoracic symptoms palliation was graded as mild, moderate and severe according to the study by Muers MF 12 and data were assessed through descriptive analysis.

Early toxicities were assessed weekly from the 1st week of starting treatment till six weeks after completion of treatment. Late toxicities were assessed after three months of the completion of treatment and thereafter every three months for a minimum period of six months using RTOG toxicity criteria.

After completion of treatment, the patients were followed up at monthly intervals, till the completion of the study period and Progression-Free Survival was assessed at the end of the study. The primary endpoints of the study were tumour response, intrathoracic symptom palliation and treatment toxicities between the two arms. Secondary endpoints include progression-free survival (PFS).

Descriptive data, such as age and median survival time, were presented as mean and standard deviation. Data on sex, stage and toxicity profile were shown as percentages and proportions. Tumour response and toxicity across groups were analysed using the chi-square test. Survival analysis was performed with the log-rank test and Kaplan-Meier curve. Statistical analysis was done using IBM SPSS Statistics, version 26. P value of<0.05 were considered as significant.

RESULTS

A total of 96 patients were recruited, with 48 in each arm. In Arm A, 4 patients defaulted the treatment due to deteriorating general conditions and also one patient opted out from the study due to personal reason. Similarly, 3 patients drop-out from the Arm B citing reasons to go outside the state for further treatment. All these defaulters were excluded from analysis and evaluation in the study. In total, 89 patients were included in the study analysis with 44 patients in Arm A and 45 patients in Arm B.

In the present study, male patients were more predominant than female patients with 26 male (59.1%) in Arm A and 24 male (53.3%) in Arm B. It was observed that most of the patient falls under the age group of 61-70 years of age with 19 patients (43.2%) in arm A and 17 patients (37.5%) in arm B. The Karnofsky Performance Status (KPS) of the patients in both the arms were observed to be 80%, seen in a total of 40 patients, 22 patients (50 %) in Arm A and 18 patients (40 %) in Arm B.

It was observed that 17 (38.6%) patients in arm A and 20 (44.4 %) in Arm B presented with Adenocarcinoma and 27 (61.4%) patients in arm A and 25 (55.6%) patients in Arm B presented with squamous cell carcinoma. Table 1 illustrates the patients characteristics and figure 1 illustrates the stage wise patient distribution in both the arms.

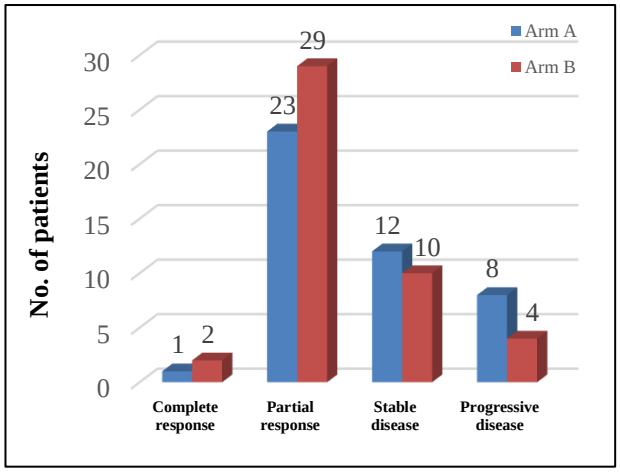

Figure 1: Treatment Response of patients in both the Arms according to the RECIST criteria after 1 month after completion of treatment.

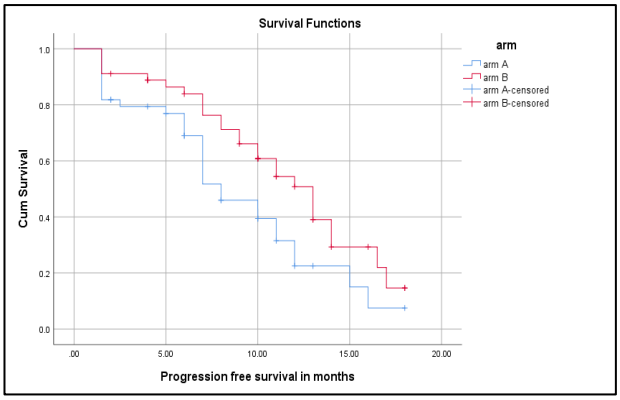

Figure 2: Kaplan-Meier curve showing progression free survival.

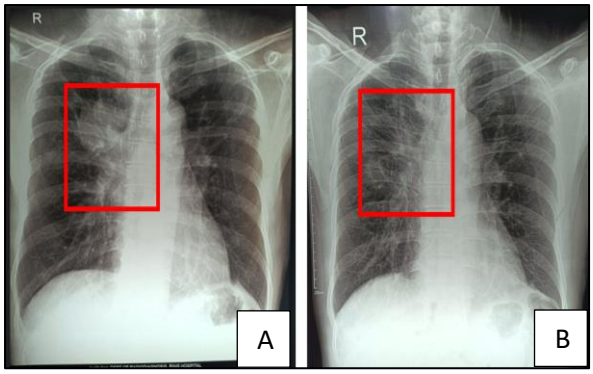

Figure 3: Anteroposterior X-Ray film of the chest wall showing partial response after the treatment (A) Pre-treatment (B) 6 weeks after completion of the treatment.

Table 2 shows the clinical presentation (Baseline symptom) of the patients at the time of first visit. It was observed that 36.4% presented with mild cough, 34.1% presented with mild chest pain, 34.1% presented with mild shortness of breath and 25% presented with mild haemoptysis in Arm A. Out of 45 patients in Arm B, 33.3% presented with mild cough, 28.9% presented with mild chest pain, 35.6% presented with mild shortness of breath and 17.8% presented with mild haemoptysis.

Table 3 show the post-treatment intrathoracic symptom palliation at 1 and 3 months after the treatment. Arm B showed 93.3% improvement in cough at 3 months, compared to 76.5% in Arm A. Chest pain improved by 96.3% in Arm B at 3 months, versus 75% in Arm A at 1 month. Shortness of breath improved by 95.7% in Arm B at 3 months, compared to 72% in Arm A. Haemoptysis improved by 90% in Arm B at 3 months, versus 83.3% in Arm A.

The p values of 0.03 for chest pain and 0.05 for shortness of breath at 3 months indicate statistical significance.

Figure 1 and table 4 shows the early treatment response after six weeks of completion of treatment. All the 89 patients (in both arms) were available for assessment. 1 patient (2.3%) shows complete response and 23 patients (52.3%) shows partial response in Arm A whereas, 2 patients (4.4%) show complete response and 29 (64.4%) patients showed partial response in Arm B. The ORR (CR+PR) was more in Arm B (68.9%) as compared to Arm A (54.5%). No response (SD+PD) was more in Arm A (45.5%) as compared to Arm B (31.1%). Disease progression (during therapy) occurred in 8 (18.2%) patients in Arm A and 4 (8.9%) patients in Arm B. The result is not statistically significant (p = 0.164).

Table 5 shows the treatment related toxicity and early side effects during treatment as per RTOG criteria. Haematological parameters, lung and oesophageal toxicity were assessed every week for 6 weeks. Esophagitis was found to be the most common side effect with 71.1% in Arm B and 68.2% in Arm A during the third week, followed by anaemia in 33.3% (Grade 1) in Arm B and 31.8% (Grade 1) in Arm A during the fifth week. The data obtained was statistically insignificant.

Table 6 shows late radiation toxicities in both arms according to RTOG criteria. Arm B had the highest rates: lung fibrosis (68.9%) and dysphagia (55.6%) at 6 months and cardiac toxicity (26.7%) at 6 months. No Grade 2 or Grade 3 toxicities for dysphagia or cardiac issues were reported in either arm. Overall, Arm B had more toxicity. No patients in either arm experienced myelitis or Esophageal stricture and most toxicities reduced upon further follow-up. The results were statistically insignificant.

Figure 2 shows progression-free survival (PFS) for both arms. The median PFS is 8 months for Arm A and 13 months for Arm B. A total of 34 patients were censored, 15 from Arm A and 19 from Arm B. The PFS difference between the arms is statistically significant, with a p value of 0.03.

Table 1: Patients characteristics of both the arms.

Patient characteristics	Arm A N (%)	Arm B N (%)
Age at diagnosis (in years)		
30-40	6 (13.6)	4 (8.9)
41-50	8 (18.2)	9 (20)
51-60	11 (25)	15 (33.3)
61-70	19(43.2)	17(37.5
Sex		
Male	26 (59.1)	24 (53.3)
Female	18 (40.9)	21 (46.7)
KPS		
60	5 (11.4)	4 (8.9)
70	5 (11.4)	9 (20)
80	22 (50)	18 (40)
90	12 (27.3)	14 (31.1)

Continued.

Patient characteristics		Arm A N (%)	Arm B N (%)
Histopathology			
Adenocarcinoma		17 (38.6)	20 (44.4)
Squamous cell carcinoma		27 (61.4)	25 (55.6)
Stage wise distribution of patients			
IIIB	T1N3MO	6 (13.6)	5 (11.1%)
	T2N3M0	8 (18.2)	10 (22.2%)
	T3N2MO	13 (29.5)	9 (20%)
	T4N2MO	9 (20.5)	9 (20%)
Total		36	33
IIIC	T3N3MO	3 (6.8)	7 (15.6%)
	T4N3M0	5 (11.4)	5 (11.1%)
Total		8	12

Table 2: Clinical presentation (baseline symptom) of the patients in both the Arms (n=89).

Symptoms	Grade	Arm A (n=44) N (%)	Arm B (n=45) N (%)
Cough	None	10 (22.7)	15 (33.3)
	Mild	16 (36.4)	15 (33.3)
	Moderate	12 (27.3)	9 (20)
	Severe	6 (13.6)	6 (13.3)
Total no. of patients with cough		34	30
Chest pain	None	20 (45.5)	18 (40)
	Mild	15 (34.1)	13 (28.9)
	Moderate	6 (13.6)	12 (26.7)
	Severe	3 (6.8)	2 (4.4)
Total no. of patients with chest pain		24	27
Shortness of breath (SOB)	None	19 (43.2)	22 (48.9)
	Mild	15 (34.1)	16 (35.6)
	Moderate	7 (15.9)	4 (8.9)
	Severe	3 (6.8)	3 (6.7)
Total no. of patients with SOB		25	23
Haemoptysis	None	32 (72.7)	35 (77.8)
	Mild	11 (25)	8 (17.8)
	Moderate	1 (2.3)	2 (4.4)
	Severe	0	0
Total no. of patients with haemoptysis		12	10

Table 3: Intrathoracic symptom palliation at 1- and 3-months post-treatment.

Month (post RT)	Symptom	Arm A N (%)	Arm B N (%)	P value
Cough				
1 month	Improvement	25/34 (73.5)	27/30 (90)	0.16
	Stable	3/34 (8.8)	2/30 (6.7)	
	Progression	6/34 (17.6)	1/30 (3.3)	
3 months	Improvement	26/64 (76.5)	28/30 (93.3)	0.17
	Stable	5/34 (14.3)	1/30 (3.3)	
	Progression	3/34 (8.8)	1/30 (3.3)	
Chest pain				
1 month	Improvement	18/24 (75)	25/27 (92.6)	0.22
	Stable	3/24 (12.5)	1/27 (3.7)	
	Progression	3/24 (12.5)	1/27 (3.7)	
	Improvement	17/24 (70.8)	26/27 (96.3)	

Continued.

Month (post RT)	Symptom	Arm A N (%)	Arm B N (%)	P value
3 months	Stable	3/24 (12.5)	1/27 (3.7)	0.03
	Progression	4/24 (16.7)	0/27 (0)	
Shortness of breath				
1 month	Improvement	17/25 (68)	20/23 (87)	0.26
	Stable	4/25 (16)	2/23 (8.7)	
	Progression	4/25 (16)	1/23 (4.3)	
3 months	Improvement	17/25 (68)	22/23 (95.7)	0.04
	Stable	3/25(12)	1/23 (4.3)	
	Progression	5/25 (20)	0/23 (0)	
Haemoptysis				
1 month	Improvement	10/12 (83.3)	8/10 (80)	0.98
	Stable	1/12 (8.3)	1/10 (10)	
	Progression	1/12 (8.3)	1/10 (10)	
3 months	Improvement	10/12 (83.3)	9/10 (90)	0.64
	Stable	1/12 (8.3)	1/10 (10)	
	Progression	1/12 (8.3)	0/10 (0)	

Table 4: Treatment Response in both the arms (n=89).

Tumour response	Treatment Arm		P value
	Arm A N (%)	Arm B N (%)	
Overall response rate (ORR) (Complete response (CR)+Partial response (PR))	24 (54.5)	31 (68.9)	0.164
No response (Stable disease (SD)+Progressive disease (PD))	20 (45.5)	14 (31.1)	

Table 5: Acute toxicity in both the Arms during treatment.

Adverse effect in weeks		Grade	Arm A N (%)	Arm B N (%)	P value
Haemoglobin					
Weeks	1-2	-	-	-	-
	3	1	10 (22.7)	13 (28.9)	0.507
	4	1	12 (27.3)	18 (40)	0.441
		2	4 (9.1)	3 (6.7)	
	5	1	14 (31.8)	15 (33.3)	0.430
		2	4 (9.1)	8 (17.8)	
	6	1	11 (25)	12 (26.7)	0.117
		2	-	4 (8.9)	
TLC					
Weeks	1-2	-	-	-	-
	3	1	4 (9.1)	5 (11.1)	0.752
	4	1	5 (11.4)	8 (17.8)	0.392
	5	1	7 (15.9)	9 (20)	0.615
	6	1	11 (25)	12 (26.7)	0.883
		2	2 (4.5)	3 (6.7)	
Platelet					
Weeks	1-3	-	-	-	-
	4	1	12 (27.3)	12 (26.7)	0.936
		2	3 (6.8)	4 (8.9)	
	5	1	10 (22.7)	10 (22.2))	0.963
		2	6 (13.6)	7 (15.6)	
	6	1	2 (4.5)	3 (6.7)	0.327
		2	0	2 (4.4)	

Continued.

Adverse effect in weeks		Grade	Arm A N (%)	Arm B N (%)	P value
Pneumonitis					
Weeks	1-3	-	-	-	-
	4	1	5 (11.4)	7 (15.6)	0.563
	5	1	7 (15.9)	9 (20)	0.615
	6	1	8 (18.2)	10 (22.2)	0.635
Esophagitis					
Weeks	1	-	-	-	-
	2	1	10 (22.7)	12 (26.7)	0.667
	3	1	30 (68.2)	32 (71.1)	0.764
	4	1	28 (63.6)	28 (62.2)	0.890
	5	1	20 (44.5)	25 (55.6)	0.341
	6	2	2 (4.5)	3 (6.7)	0.664

Table 6: Late radiation toxicity in both the two arms according to RTOG criteria.

Adverse effects		Arm A N (%)	Arm B N (%)	P value
Lung fibrosis				
Month 3	Grade 1	25 (56.8)	26 (57.8)	0.926
	Grade 2	4 (9.1)	5 (11.1)	
	Grade 3	0	0	
Month 6	Grade 1	30 (68.2)	31 (68.9)	0.883
	Grade 2	3 (6.8)	2 (4.4)	
	Grade 3	0	0	
Month 9	Grade 1	25 (56.8)	28(62.2)	0.845
	Grade 2	4 (9.1)	3 (6.7)	
	Grade 3	0	0	
Dysphagia				
Month 3	Grade 1	12 (27.3)	13 (28.9)	0.865
Month 6	Grade 1	20 (45.5)	25 (55.6)	0.341
Month 9	Grade 1	14 (31.8)	18 (40)	0.421
Cardiac toxicity				
Month 3	Grade 1	10 (22.7)	12 (26.7)	0.667
Month 6	Grade 1	11 (25)	12 (26.7)	0.857
Month 9	Grade 1	10 (22.7)	11 (24.4)	0.849
Myelitis and esophageal stricture	-	-	-	-

DISCUSSION

Despite advances in systemic treatments and modern radiotherapy, local control and survival in patients with locally advanced NSCLC remain limited.[13]

For stage III patients unable to undergo radical treatment and stage IV patients with good performance status, treatment aims focus on symptom management, improving quality of life and extending survival. Therapy decisions consider factors like PDL-1 expression, driver mutations, tumour histology, disease extent and symptoms.[9]

These patients often experience mild to severe symptoms from intrathoracic disease, affecting their quality of life and face potential complications from local disease progression. Thus, local treatment alongside systemic therapy is clinically essential.[14]

The present study is designed similarly to the one conducted by Lehman et al, with the key difference being the use of Nab-paclitaxel, a nanoparticle albumin-bound form of paclitaxel, which is known to have fewer side effects compared to solvent-based paclitaxel.[9] Here, 89 cases of LA-NSCLC patients were randomised and a comparison was made between Arm A consisting of 44 patients and Arm B consisting of 45 patients.

In the present study, male were more predominant than female with 59.1% in Arm A and 53.3% in Arm B. These findings are consistent with the studies conducted by Chiang et al and Bezjak et al.[15,16] Majority of the patients fall in the age range of 61-70 years with 43.2% in arm A

and 37.5% in arm B. It validates that lung cancers usually occur in older age group patients. These findings are comparable to the findings by Thandra et al, where the average age for lung cancer diagnosis in the US was 70 years and also the study by Chiang et al, which had a median age of age of 62 years old (range, 41–87 years).[15,17] The performance status of the study population was maximum in 80% KPS with 50% from Arm A and 40% in Arm B which is consistent with the study by Prasad et al.[18]

In the present study, Arm A had 81.9% patients in Stage IIIB and 18.1% in Stage IIIC. Arm B had 73.3% patients in Stage IIIB and 26.7% in stage IIIC. The stage distribution percentage is lesser compared to the study percentages predicted by Casal-Mouriño et al.[19]

The histopathological type most commonly presented in the present study was squamous cell carcinoma with 61.4% in arm A and 55.6% in arm B, which is similar to the study conducted by Casal-Mouriño et al, but contrary to the study conducted by Chiang Y et al.[15,19]

The baseline intrathoracic symptom presentation was almost similar in both Arm A and Arm B with cough being the most common presentation, followed by chest pain, shortness of breath and haemoptysis. It was similar to the study conducted by Buccheri et al.[20] Literature review on symptomatology reveals the varied symptomatic presentation of patients suffering from lung cancer. The most common symptoms include cough, weight loss, dyspnoea, chest pain and haemoptysis, while rarer symptoms include stridor, voice changes, dysphagia, fatigue, anorexia, superior vena cava obstruction and pain in other body part, which was similar to our present study. Chest pain in lung cancer may result from discomfort due to enlarged lymph nodes, invasion to the chest wall and the lining around the lungs called pleura.[21,22] Intrathoracic symptom palliation was assessed at 1st and 3rd months after the treatment in both the study arms.

The 6-weeks' time point was selected because it was anticipated that the greatest symptomatic improvement would occur at this time.[9] 93.3% of the patients presenting with cough in Arm B had improvement compared to 76.5% in arm A at 3 months post treatment. 96.3% of the patients presenting with chest pain had improvement in Arm B at 3 months of the follow up compared to 75% in Arm A at 1 month. 95.7% of the patients presenting with shortness of breath shows improvement in Arm B at 3 months compared to 72% in Arm A.

90% of the patients presenting with haemoptysis in Arm B reported improvement at 3 months of follow up compared to 83.3% in Arm A. Palliation of symptom was slightly better in Arm B, though early palliation was achieved in Arm A for Haemoptysis at 1 month.

Both treatment arms provided effective palliation of individual symptoms with statistically significant difference in chest pain (p=0.03) and shortness of breath (p=0.05) between the two arms. Overall, symptom palliation in the present study was better as compared to the study conducted by Lehman et al and the most effectively palliated symptoms in our study were chest pain and shortness of breath as opposed to chest pain and haemoptysis by other authors.[9,23,24]

Treatment response by radiological imaging for both the arms reveal that 2.3% had complete response and 52.3% had partial response in Arm A with an overall response rate of 54.6%. 4.4% had complete response and 64.4% had partial response with an overall response rate of 68.8% in Arm B. The response rate in Arm B is almost similar with the study conducted by Michael et al, where the overall response rate comes to 65%, stable disease to 17% and progressive disease was noted in 9% of the study population.[25] Our study had a better overall response rate in arm B when compared to the study conducted by Burmeister et al, which might be due to better compliance to Nab-paclitaxel chemotherapy in NSCLC patients.[26,27]

In the present study, acute toxicities were mostly observed after 3 weeks of the start of treatment in both the arms. Haematological toxicities were present in both the arms which were comparable, with anaemia seen in 33.3% of the patient in Arm B and 31.8% in Arm A in fifth week of treatment.

Leukopenia was prominent in 26.7% of the patient in Arm B as compared to 25% in Arm A at sixth weeks of treatment. Grade I thrombocytopenia was seen in 27.3% of the patient in Arm A as compared to 26.7% in Arm B during the fourth week of treatment. Our study findings were similar to the study done by Atagi et al, and Dawe et al, where haematological toxicities were more in the concurrent chemotherapy arm.[28,29] Grade I pneumonitis and esophagitis were also observed in both the treatment groups, with pneumonitis becoming prominent by the fourth week of treatment and gradually increased over the treatment period with 22.2% in Arm B and 18.2% in arm A by the end of six weeks.

Esophageal toxicities were seen maximum at three weeks of the treatment with 71.1% in Arm B and 68.2% in Arm A. By six weeks, 6.7% in Arm B and 4.5% in Arm A had grade 2 esophageal toxicity. Our study shows lesser esophagitis and pneumonitis as compared to the study done by Wu et al, where esophagitis and pneumonitis was seen in 75% and 50% of the patient respectively.[30] In all cases, these toxicities were reversible and was managed conservatively. Thus, it was observed that acute radiation toxicities were more in Arm B but it was manageable.

The incidence of late radiation side effects were assessed at 3, 6 and 9 months of treatment completion with minimum follow up of 6 months. Maximum incidence of grade 1 lung fibrosis was almost equal in both the arms. Arm B (68.9%) and Arm A (68.2%) at six month of follow up. Dysphagia was prominent at six months of follow up at 55.6% in Arm B and 45.5% in Arm A.

This result is contradictory to the study by Abbas et al, where 39.3% incidence of radiation fibrosis and only 7.1% of dysphagia was reported.[31] Utilization of two-dimensional radiation therapy in our centre could be a contributing factor to the higher percentage of lung fibrosis and dysphagia. Cardiac toxicity was almost equal in both the arms in our study at approximately 26%. There is very less study about the cardiac radiation dose analysis in relation to lung cancer.

A study conducted by Schytte et al, did not find any relation between high mean-dose to different volumes of the heart and cardiac toxicity.[32] Another study conducted by Atkins et al, noted that the radiation dose exposure to the heart is a modifiable cardiac risk factor for major adverse cardiac events (MACE) and all-cause mortality (ACM), supporting the need for early recognition and treatment of cardiovascular events and more stringent avoidance of high cardiac radiotherapy dose.[33] More study is needed in order to identify the events, volume, dose and relationship between cardiac events and lung cancer radiation therapy in specific subsets of patients. In the present study, the median progression free survival (PFS) was 8 months in Arm A and 13 months in Arm B. The difference in PFS was statistically significant with a p value of 0.03. These findings were higher to the study done by Sarihan S et al, where the median PFS was 6 months in the RT arm and 9 months in the CCRT arm.[34] Our findings were almost similar with the study by Tsuchiya-Kawano et al, where the median PFS was given at 11.3 months.[11]

CONCLUSION

Our present study was designed in palliative settings to analysed whether addition of nab-paclitaxel in concurrent chemotherapy would increase the tumour response as opposed to platinum-based chemotherapy which is the standard chemotherapy but with higher toxicities for the patients.

In our study, the overall response after the treatment completion was better in Arm B (68.8%) as compared to Arm A (54.6%). Both arms showed intrathoracic symptom palliation, with Arm B demonstrating a higher percentage of palliation. The most common symptom which was palliation was for chest pain (p value=0.03) and shortness of breath (p value=0.04), followed by cough and haemoptysis. Arm B exhibited more pronounced acute and late radiation toxicities; however, they were manageable. Progression free survival was found to be better in Arm B as compared to Arm A (p value=0.03). In conclusion, Arm B demonstrated better results, but in totality, the two palliative lung cancer treatment regimens were almost equal in efficacy in terms of radiological response of the primary tumour, intrathoracic symptom palliation and toxicity. However, further researches with larger study population and a longer study period have to be conducted to confirm the positive results obtained from this study. All the patients in our study tolerated the treatment well and complications were handled easily without interruption of treatments.

The limitations of our study were: small sample size, limited follow-up time, treatment with 2D Cobalt-60 teletherapy machine. Long term follow-up with bigger sample size and comparative trials are needed for further analysis in regards to tumour response, toxicities and intrathoracic symptom palliation to provide definitive conclusions whether palliative concurrent chemotherapy radiotherapy is better or in par with palliative radiotherapy alone for the treatment of locally advanced inoperable non-small cell lung cancer.

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