www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i6.210

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research

Palliative Radiotherapy with Concomitant and Maintenance Gefitinib for the Management of Locally Advanced Adenocarcinoma Lung Patients Unfit For Radical Treatment

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ABSTRACT

Purpose: *To evaluate the feasibility and role of palliative radiotherapy and concomitant gefitinib and maintenance in locally advanced adenocarcinoma lung patients unfit for radical radiotherapy with respect to symptomatic relief with improvement in quality of life, local control, toxicity, progression free survival (PFS) & overall survival (OS).*

Material and Methods: *A total of thirty four (34) patients with stage III adenocarcinoma lung were accrued in the study who presented in the Department of Radiotherapy, PGIMS Rohtak from January 2015 to June 2016. Presenting symptoms were cough in 18, breathlessness in 23, expectoration with blood in 4 and chest pain in 24 patients. Male:female was 20:14. All accrued patients had KPS 40 to 60. These patients were treated with palliative EBRT 30 Gy in 10 fractions over 2 weeks and oral Gefitinib 250 mg once a day, from the first day of radiotherapy, concomitant & continued thereafter till disease progression. Median follow-up was 7 months (range 2-24 months). The patients were assessed for symptomatic relief, local control, toxicity, progression free survival & overall survival.*

Results: *All patients had tolerated the treatment well and no significant drug induced toxicity was observed. More than ≥25% relief in cough, chest pain, haemoptysis and dyspnoea was observed in 55%, 54%, 100% & 74% of patients respectively. Partial response was observed in 68% patients while remaining had stable disease at 1st follow up. At 6th follow up, 38% & 12% patients maintained their partial response and stable disease status respectively. Diarrhoea and skin rashes were two toxicities which were observed in 38% and 59% patients. Median PFS & OS were 6 months (range 2 – 24 months) and 7 months respectively. Prognostic factors like smoking, EGFR overexpression, pre and post treatment quality of life were statistically significant in improving the OS (p-value 0.0010, 0.0031, 0.006, 0.0001 respectively). EGFR overexpression status and post-treatment quality of life were also found to be statistically significant in improving the PFS (p-value<0.0001 and 0.0004 respectively).*

Conclusion: *The present study demonstrates the favourable safety profile, ease of administration and a promising outcome in terms of results attained with palliative radiotherapy concurrent with gefitinib, in adenocarcinoma lung patients presenting with locally advanced stage not amenable to radical radiotherapy. However, the results need to be warranted by future studies with the larger samples in order to recommend it as a standard protocol.*

INTRODUCTION

In developed countries, we can expect from the patients of carcinoma lung to present in early stages (stage I & II). But in developing countries like India, most of the patients present in locally advanced as well as in metastatic stage[1,2], due to the lack of awareness, economic constraints and most importantly asymptomatic early stages of the disease causing their late presentation.

Patients presenting with metastatic stage of carcinoma lung require management based upon the site of metastasis mainly. But patients in locally advanced stage (stage III) present a unique kind of challenge about their management. In most of the cases, these patients are unfit for surgery as well as concomitant chemo-radiotherapy due to already locally advanced nature of the disease hampering the pulmonary functions, causing moderate to severe symptomatic distress, degrading their performance status.[2,3,4] So, palliative radiotherapy comes into picture for immediately relieving the symptomatic distress.[3] At the same time, adenocarcinoma histology of lung cancer provides us a specific target i.e. Epithelial Growth Factor Receptor (EGFR).[5,6] Drugs like gefitinib acting as EGFR-Tyrosine kinase inhibitors (TKIs) have already proven their efficacy in the management of adenocarcinoma lung.[7] Gefitinib has radiosen-sitizing effect in EGFR mutation positive lung adenocarcinoma and the prevalence of this mutation in adenocarcinoma is ~50% of Asian patients.[8,9]In order to enhance the effect of palliative radiation therapy and decrease the toxicity as compared to radical radiotherapy, it may be beneficial if radiation therapy and EGFR inhibitors may be administered concurrently to the patients of adenocarcinoma lung presenting in locally advanced stage who are unable to tolerate the radical intent treatment.

So, the present study of combining the gefitinib with palliative radiotherapy and continuing the gefitinib alone as maintenance therapy was designed to evaluate symptomatic relief, local control, quality of life, progression-free survival (PFS) and overall survival (OS) in patients with locally advanced adenocarcinoma lung unfit for radical treatment.

PATIENTS & METHODS

Patient characteristics & pre-treatment evaluation

The study was conducted on 34 previously untreated, histopathologically proven patients of locally advanced adenocarcinoma lung reporting in the Department of Radiotherapy, Pt. B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak between January, 2015 to June 30, 2016 where radical treatment was not feasible. Inclusion criteria are enumerated in Table 1. Due to lack of proper tissue samples, confirmed EGFR mutation status was not considered as inclusion criteria. The pre-treatment evaluation in all patients included complete history, general physical examination and complete systemic examination. Severity of presenting symptoms was assessed using Percentage Method (Annexure 1).

Radiological assessment including chest X-ray PA view and lateral view, CECT Chest, USG abdomen and pelvis for metastatic disease was done in all patients. To assess the quality of life, FACT-G (Functional assessment of cancer therapy- General) scoring was done on first day of presentation of the patient in OPD and also after the four weeks of completion of palliative radiotherapy concomitant with gefitinib. Table 2 is showing the details about the patient characteristics.

Table 1. Inclusion Criteria

- Karnofsky Performance Status <70 to >30
- Complete haemogram with Hb>8gm/dL; TLC>4000/cmm, Platelet count >100,000/cmm.
- Renal function tests with Blood urea < 40mg/dL and Serum creatinine < 1.5mg/dL.
- Liver function tests with SGOT < 35 IU/L and SGPT < 40 IU/L.
- AJCC stage III and a positive biopsy/cytology of lung adenocarcinoma.
- Patients who sign the informed consent and are ready to be on follow up as required.

Table 2: Patient characteristics

Characteristics	n	%
Age (years)		
Median	60	
Range	38 - 74	
Gender		
Male	20	59
Female	14	41
Male:Female	1.41	
Rural/urban status		
Rural	28	82
Urban	6	18
Smoker		
Male	16	47
Female	2	6
Non-smoker		
Male	4	12
Female	12	35
KPS		
60	22	65
50	10	30
40	2	5
Symptoms at presentation		
Cough	18	53
Breathlessness	23	68
Chest pain	24	71
Blood in sputum	4	12
Stage		
IIIA	9	26
IIIB	25	74
FACT-G Score		
61-70	10	29
71-80	20	59
81-90	4	12
91-100	0	0
101-110	0	0
Mean	73.41	
EGFR status		
Present	11	32
Males (Smoker + Non-smoker)	9 (5 + 4)	
Females (Smoker + Non-smoker)	2 (0 + 2)	68
Not available	23	
Males (Smoker + Non-smoker)	11 (11 + 0)	
Females (Smoker + Non-smoker)	12 (2 + 10)	

METHODOLOGY

All the patients were given gefitinib 250 mg orally 3 hours before radiotherapy each day from the first day of starting the radiotherapy. The dose of palliative radiotherapy 30 Gy in 10 fractions over a period of 2 weeks with each fraction of 3 Gy over 5 continuous days a week was given to the patient. Then gefitinib 250 mg a day orally was continued for every patient during follow up till the evidence of disease progression.

Assessment during the treatment & in follow up period

Weekly assessment of adverse events was done by Radiation Therapy Oncology Group (RTOG) criteria and WHO toxicity criteria during the palliative radiotherapy. Patients were assessed thoroughly four weeks after the completion of palliative radiotherapy with concomitant with gefitinib. Subjective relief in symptoms was assessed using Percentage Method (Annexure 1). Quality of life was assessed by FACT-G (Functional assessment of cancer therapy-General). Tumour response was determined by using CECT Chest and assessed by using WHO response criteria. Treatment related toxicity was graded using RTOG criteria. Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria was utilized for acute reactions. Patients were followed up monthly on OPD basis for a period of at least six months. At every visit, each patient was clinically evaluated for symptomatic relief, local control of disease and treatment related complications. The patients were assessed for any evidence of distant metastasis during each follow up. Response was assessed by serial x-ray studies and CT scan if needed.

Statistical analysis

The data thus obtained was assessed and analysed in terms of symptomatic relief, improvement in quality of life, local tumour response, toxicity profile and survival. Significant improvement in quality of life was determined statistically using T-test (two-tailed). Cox proportional hazard regression was used to determine the impact of quality of life in improving the survival. Progression Free Survival (PFS) and Overall Survival (OS) were determined using Kaplan Meier curves. Log-rank test was used to test the significance of different survival curves. All statistical work was done using MedCalc® Software version 16.8.4.

RESULTS

Subjective Relief in symptoms

Subjective relief in cough

At first follow up, patients who got ≥25% relief in cough were fifty five percent and who got less than 25% relief were forty five percent, among the patients having cough as the presenting symptom. Eleven percent patients got very good relief while similar percentage of patients got good relief. Nearly one third patients got moderate relief. Table 3 is representing the details about the status of relief in cough during follow up period.

Subjective relief in breathlessness

Patients who got ≥25% relief in breathlessness were seventy four percent at first follow up. Twenty six percent of symptomatic dyspnoeic ones got poor relief while fifty two percent got very good relief. Table 3 is representing the details about the status of relief in breathlessness during follow up.

Subjective relief in Chest pain

Fifty four percent patients, among the patients who had chest pain as the presenting symptom, got ≥25% relief in chest pain at first follow up. There were forty six percent patients who got poor relief even after the treatment. Twenty nine of the patients got very good while 8% got only good relief. Table 3 is representing the details about the status of relief in chest pain during follow up.

Subjective relief in blood in sputum

All of the patients got ≥50% relief in blood in sputum whose presenting symptom was blood in sputum. Table 3 is representing the details about the status of relief in chest pain during follow up.

Table 3 Number of patients with category of subjective relief at each follow up

Category of relief		Poor relief	Moderate relief	Good relief	Very good relief	Death of patients during FU	Total number of patients living cough
Relief in cough (N)	1st FU	8	6	2	2	0	18
	2nd FU	7	3	1	2	5	13
	3rd FU	7	2	0	2	2	11
	4th FU	7	3	0	0	1	10
	5th FU	7	3	0	0	0	10
	6th FU	8	2	0	0	0	10
Relief in breathlessness (N)	1st FU	6	2	3	12	0	23
	2nd FU	8	0	1	12	2	21
	3rd FU	7	4	0	8	2	19
	4th FU	11	3	0	5	0	19
	5th FU	13	3	0	2	1	18
	6th FU	14	2	0	2	0	18
Relief in chest pain (N)	1st FU	11	4	2	7	0	24
	2nd FU	13	4	2	5	0	24
	3rd FU	13	9	2	0	0	24
	4th FU	18	6	0	0	0	24
	5th FU	19	5	0	0	0	24
	6th FU	21	3	0	0	0	24
Relief in blood in sputum (N)	1st FU	0	0	2	2	0	4
	2nd FU	0	0	2	2	0	4
	3rd FU	0	0	2	2	0	4
	4th FU	0	0	2	2	0	4
	5th FU	0	0	2	2	0	4
	6th FU	0	0	2	2	0	4

Quality of life analysis

Statistical analysis using T-test (two-tailed) compares both the pre-treatment as well as post-treatment FACT-G Scores, showed significant improvement in quality of life following the treatment. Figure 1 & Table 4 are representing the details about the statistical analysis.

Figure 1

Comparative graph of pre and post-treatment FACT-G scores

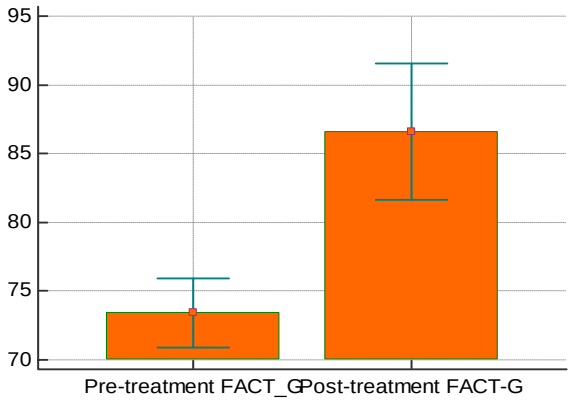


Table 4

Statistical analysis between pre and post-treatment FACT-G scores

	Pre-treatment FACT-G	Post-treatment FACT-G
Sample size	34	34
Arithmetic mean	73.4118	86.5882
T-test (assuming equal variances) Two-tailed probability	p value < 0.001 (significant)	

Toxicity assessment

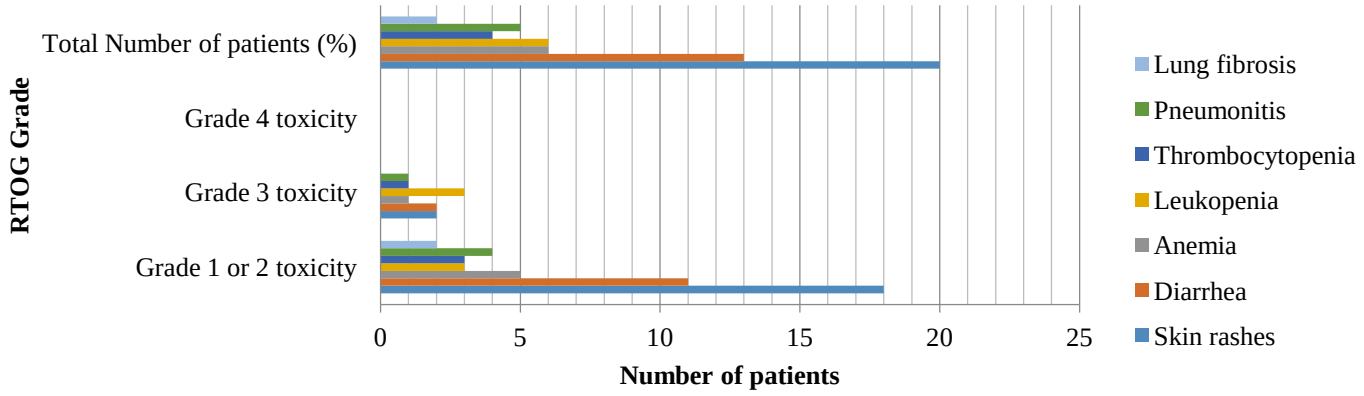
Skin rashes were the most common toxicity, encountered in 59% of the patients. Among the patients having skin rashes, only 2 patients had grade 3 skin rashes and none had grade 4. Second most common toxicity observed was diarrhoea in 38% of the patients. Among them, only 2 patients had grade 3 diarrhoea and none was having grade 4 diarrhoea. Haematological toxicities were also observed in small number of patients. Leukopenia

was seen in 18% of the patients, without grade 3 or 4 toxicity. Thrombocytopenia was seen in 12% of the patients, among which 1 patient had grade 3 thrombocytopenia and none had grade 4. Anaemia was observed in 18% of the patients, among which 1 patient had grade 3 toxicity and no grade 4 toxicity. Both radiation-induced pulmonary pneumonitis and lung fibrosis were also noticed in 15% and 6% of the patients respectively, with no grade 3 or 4 toxicity. Table-5& Figure 2 show the total number of patients having treatment related toxicities.

Table-5 Overall toxicities of the treatment during 6 month follow up period

Toxicity	Grade 1 or 2 toxicity	Grade 3 toxicity	Grade 4 toxicity	Total Number of patients (%)
Skin rashes	18	2	0	20 (59)
Diarrhea	11	2	0	13 (38)
Anemia	5	1	0	6 (18)
Leukopenia	3	3	0	6 (18)
Thrombocytopenia	3	1	0	4 (12)
Pneumonitis	4	1	0	5 (15)
Lung fibrosis	2	0	0	2 (6)

Figure 2
Overall toxicities of the treatment during 6 month follow up period



Tumour response to the treatment

Tumour response after 1 month of Follow up

Sixty eight percent patients had shown partial response to the treatment while 32% patients had maintained stable disease status. Not even a single patient had shown progressive disease nor any patient died in 1 month following the treatment.

Tumour response after 6 months of follow up

Lung carcinoma again proved it to be a great burden on mankind, as 24% of patients were already died and 29% showed disease progression within 6 months of follow up. Thirty eight percent patients who had shown partial response and 18% who had maintained stable disease status even after 6 months was a sigh of relief.

Progression free survival (PFS) & Overall Survival (OS)

Median follow up period was 7 months (range 2 – 24 months). Median PFS was 6 months (range 1 – 16 months). The present study also provided the overall survival of 32 patients among the total of 34 patients who were treated as the two patients were still alive at the point of compilation of results. The median overall survival (OS) was 7 months (range 2 – 20 months). Figure-3 is showing Kaplan Meier curves of progression free survival (PFS) and overall survival (OS).

Evaluation of prognostic factors

Impact of gender on overall survival

Univariate analysis demonstrated that gender of the patient has no statistically significant relation

with overall survival. Female patients have shown better survival than male patients but the difference was statistically non-significant (p = 0.06). Figure 4 shows the survival curves of both male (M) and female (F) patients

Impact of smoking status on overall survival

Univariate analysis demonstrated that smoking status has statistically significant relation with overall survival. Non-smokers have significant survival advantage over smokers (p = 0.0010). Figure-5 shows the survival curves of smoker (S) and non-smoker (NS) patients.

Impact of EGFR overexpression status on Progression Free Survival (PFS)

Univariate analysis demonstrated that EGFR overexpression status has statistically significant relation with Progression Free Survival (PFS). Patients who had confirmed EGFR overexpression status have significant PFS advantage over the patients having non-available EGFR overexpression status (p = <0.0001). Figure-6 shows the survival curves of confirmed EGFR overexpression (Present) and non-confirmed EGFR overexpression status (Non-available) comparing them side by side.

Impact of EGFR overexpression status on overall survival

Univariate analysis demonstrated that EGFR overexpression status has statistically significant relation with overall survival. Patients who had confirmed EGFR overexpression status have significant survival advantage over the patients having non-available EGFR overexpression status (p = 0.0031). Figure-7 shows the survival curves of confirmed EGFR overexpression (Present) and non-confirmed EGFR overexpression status (NA) comparing them side by side.

Figure 3

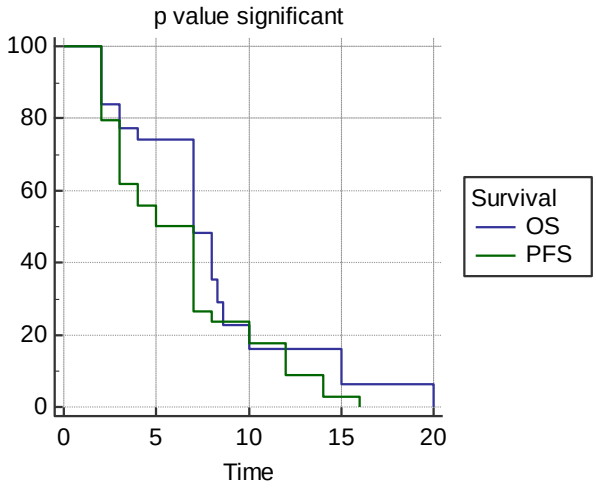


Figure 4

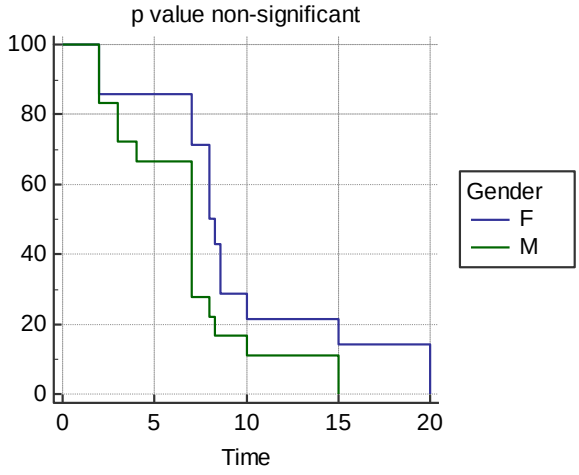


Figure 5

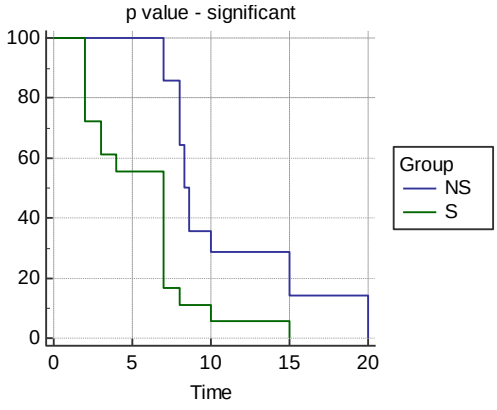


Figure 6

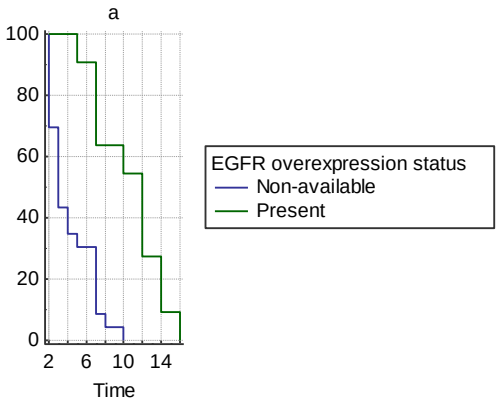


Figure 7

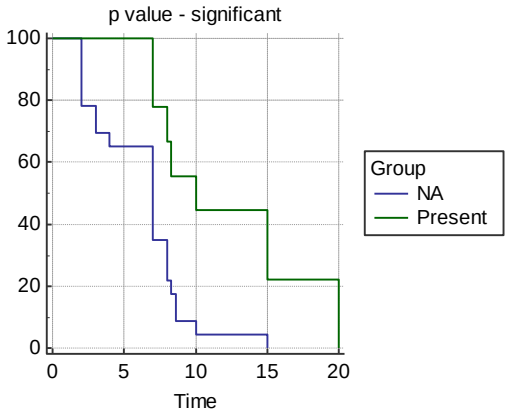


Figure 3-7. Kaplan Meier curves showing (3) - Progression Free Survival (PFS) and Overall Survival (OS), (4) - Impact of gender on overall survival, (5) - Impact of smoking on overall survival, (6) - Impact of EGFR overexpression status on Progression Free Survival, (7) - Impact of EGFR overexpression status on overall survival

Relation between Quality of life and survival

Post-treatment quality of life is associated with improvement in PFS and that is statistically significant (p = 0.0004). Pre-treatment quality of life is also associated with improvement in PFS but non-statistically significant. Table-6 shows the hazard ratio and p-value, obtained using cox proportional hazard ratio. Both Pre and Post-treatment quality of life is associated with improvement in Overall Survival (OS) and that is statistically significant (p = 0.0068 and 0.0001 respectively). Table-7 shows the hazard ratio and p-value, obtained using cox proportional hazard ratio.

Table-5 Effect of pre-treatment as well as post-treatment FACT-G score on Progression Free Survival (PFS) (showing Hazard Ratio and p value)

Covariate	p value	HR (95% CI)
Post-treatment FACT-G	0.0004	0.9145 to 0.9748
Pre-treatment FACT-G	0.1638	0.8956 to 1.0189

Table-6 Effect of pre-treatment as well as post-treatment FACT-G score on Overall Survival (OS) (showing Hazard Ratio and p value)

Covariate	p value	HR (95% CI)
Post-treatment FACT-G	0.0001	0.8718 to 0.9533
Pre-treatment FACT-G	0.0068	0.8591 to 0.9760

DISCUSSION

For carcinoma lung patients, even after the decades of development of a lot of modalities for delivering radiation therapy more efficiently and a number of new molecules for targeting the carcinomatous cells, improvement in much survival is still awaited.[10]This prospective, open label study has been conducted to evaluate the role of palliative radiotherapy with concomitant and maintenance gefitinib, with respect to symptomatic relief & improvement in quality of life, tolerability & toxicity profile and local control in locally advanced adenocarcinoma lung patients which were unsuitable for radical treatment.

The most significant thing that was observed in the study was symptoms with which the patient presented and among them, the stress was given to those symptoms which were the main culprit of degrading the quality of life of the patients. Chest pain was the most common among them, 71% of

the patients were presented with the same. Breathlessness and cough were next in ranks, with 68% and 53% of the patients having breathlessness and cough respectively. Blood in sputum was also the presenting symptom but only in few numbers of patients (12%). On the basis of Lung Cancer Symptoms Scale, Iyer et al. also proved that the above mentioned lung cancer specific symptoms are the most common to present, affecting the quality of life.[11]

Patients who got ≥25% relief in cough were 55%. So the remaining 45% of the patients got less than 25% relief. Very good relief in cough was also observed but in 11% of the patients and similar percentage i.e. 11% of the patients also got good relief. Nearly one third of the patients got moderate relief in cough. Patients who got ≥25% relief in breathlessness were 74%. 26% of symptomatic dyspnoeic ones got poor relief. 52% of the patients achieved very good relief. 13% of the patients got good relief and 9% got moderate relief while 26% of the patients got poor relief in breathlessness. Among the patients having chest pain as the presenting symptom, 54% of the patients got ≥25% subjective relief in chest pain. Remaining 46% of the patients got poor relief in the chest pain. 29% of the patients got very good while 8% got only good relief in chest pain. Blood in sputum was the presenting complaint in few patients, comprising 11.8% of the total. After the treatment, all the patients having this complaint got either good (50% of the patients) or very good relief (remaining 50%). Symptomatic relief achieved by the study can be compared with the analysis of 1250 patients with non-small cell lung cancer treated with palliative radiotherapy only; relief of symptoms was observed in 54% of patients for the cough, 68% for haemoptysis, 51% for chest pain and 38% for dyspnoea.[12]

Post-treatment FACT-G Scores analysis in present study showed statistical significant improvement in quality of life following the treatment. Same schedule of thoracic radiotherapy was used by Sau et al. for pain palliation and health-related quality of life using FACT-G in non-small cell lung carcinoma patients but improvement in FACT-G score was statistically non-significant.[13]But statistically significant improvement in FACT-G Score in present study shows the promising role of adding gefitinib in the radiotherapy during palliative setting in adenocarcinoma lung patients.

Impact of gefitinib concomitant with palliative radiotherapy as well as maintenance therapy with gefitinib in terms of adverse effects observed in the present study found that skin rashes were the most common toxicity, encountered in 59% of the patients. Among the patients having skin rashes, only 2 patients had grade 3 skin rashes and none had grade 4. Second most common toxicity observed was diarrhoea in 38% of the patients. Among them, only 2 patients had grade 3 diarrhoea and none was having grade 4 diarrhoea. Haematological toxicities were also observed in small number of patients. Leukopenia was seen in 18% of the patients, without grade 3 or 4 toxicity. Thrombocytopenia was seen in 12% of the patients, among which 1 patient had grade 3 thrombocytopenia and none had grade 4. Anaemia was observed in 18% of the patients, among which 1 patient had grade 3 toxicity and no grade 4 toxicity. Both radiation-induced pulmonary pneumonitis and lung fibrosis were also noticed in 15% and 6% of the patients respectively, with no grade 3 or 4 toxicity. Skin rashes, diarrhoea and haematological toxicities were less while late complications like radiation-induced pneumonitis and lung fibrosis were more in present study as compared to study by Wang et al.[5] Difference in rate of complications was due to use of conventional fraction and curative intent of treatment by Wang et al.[14]

On CECT chest, sixty eight percent patients had shown partial response to the treatment while 32% patients had maintained stable disease status at first follow up. Not even a single patient had shown progressive disease nor any patient died in 1 month following the treatment. Every patient was evaluated for tumour control during subsequent follow ups using chest x-ray and if required CECT chest. Lung carcinoma again proved it to be a great burden on mankind, as 24% of patients were already died and 29% showed

disease progression within 6 months of follow up. Thirty eight percent patients who had shown partial response and 18% who had maintained stable disease status even after 6 months, was a sigh of relief.

Median follow up period of the present study was 7 months (range 2 – 24 months). Median Progression Free Survival (PFS) and median overall survival (OS) were 6 months (range 1 – 16 months) and 7 months (range 2 – 20 months) respectively. Nearly similar Progression Free Survival (PFS) of 5.5 months was observed by a meta-analysis of 2334 patients of non-small cell lung carcinoma from 5 randomised trials.[15]Median overall survival (OS) of 7 months was observed by a retrospective review[16] of the prospective database of all the patients of non-small cell lung carcinoma. in which neoadjuvant chemotherapy followed by radiotherapy was givenbut in present study, the same median survival was achieved with palliative radiotherapy concomitant and maintenance with gefitinib.

Univariate analysis demonstrated that gender of the patient has no statistically significant relation with overall survival. Female patients have shown better survival than male patients but the difference was statistically non-significant (p = 0.06). But Wang et al observed that female gender had statistically significant effect on survival as compared to male gender.[14] Small sample size and less number of female patients in present study was the reason for observing statistically non-significant difference in survival on the basis of gender.

Relationship between various prognostic factors and overall survival was also observed. Factors like smoking status, EGFR overexpression status and pre-treatment as well as post-treatment quality of life were statistically significant in improving the overall survival (p-value 0.0010, 0.0031, 0.006 and 0.0001 respectively). Pre-treatment quality of life is a statistically significant predictor of survival for patients with advanced lung cancer, also confirmed by Dharma-Wardene et al.[17]

EGFR overexpression status and post-treatment quality of life were also found to be statistically significant in improving the progression free survival (PFS) (p-value <0.0001 and p-value 0.0004 respectively). Pre-treatment quality of life is also associated with improvement in PFS but non-statistically significant.

In conclusion, the present study demonstrates the favourable safety profile, ease of administration and a promising outcome in terms of results attained with palliative radiotherapy concurrent with gefitinib, in adenocarcinoma lung patients presenting with locally advanced stage not amenable to radical radiotherapy. However, the results need to be warranted by future studies with the larger samples in order to recommend it as a standard protocol.

REFERENCES

1. Singh N, Aggarwal AN, Gupta D, Behera D, Jindal SK. Unchanging clinic-epidemiological profile of lung cancer in north India over three decades. Cancer Epidemiol. 2010;34:101-4.
2. Agrawal S. Challenges in optimizing chemoradiation in locally advanced non-small cell lung cancers in India. South Asian Journal of Cancer. 2013;2(4):265-71.
3. Behera D, Balamugesh T. Lung cancer in India. Indian J Chest Dis Allied Sci. 2004;46:269-81.
4. Chang YJ, Bradley JD, Govindan R, Komaiki R. Lung. In: Halperin EC, Perez CA, Brady LW, editors. Perez and Brady's Principles and Practice of Radiation Oncology. 5th ed. Philadelphia: Lippincott Williams & Wilkins. 2008. p. 1079.
5. Stella GM, Luisetti M, Pozzi E, Comoglio PM. Oncogenes in non-small cell lung cancer: emerging connections and novel therapeutic dynamics. Lancet Respir Med. 2013;1:251-61.
6. Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, et al. Gefitinib or carboplatin/paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361:947-57.

7. Cohen MH, Williams GA, Sridhara R, Chen G, Pazdur R. FDA drug approval summary: gefitinib (ZD1839) (Iressa) tablets. Oncologist. 2003;8:303-6.
8. Tanaka T, Munshi A, Brooks C, Liu J, Hobbs ML, Meyn RE. Gefitinib radiosensitizes non-small cell lung cancer cells by suppressing cellular DNA repair capacity. Clin Cancer Res. 2008;14(4):1266-73.
9. Finberg KE, Sequist LV, Joshi VA, Muzikansky A, Miller JM, Han M, et al. Mucinous differentiation correlates with absence of EGFR mutation and presence of KRAS mutation in lung adenocarcinomas with bronchioloalveolar features. J Mol Diagn. 2007;9:320-6.
10. Majumdar. Stem cells and cancer. Online-Ausg. ed. New York: Springer. 2009. p.193.
11. Iyer S, Roughley A, Rider A. The symptom burden of non-small cell lung cancer in USA. Support Care Cancer. 2014;22:181-7.
12. Reinfuss M, Mucha-Maecka A, Walaswk T, Blecharz P, Jakubowicz J, Skotnicki P, et al. Palliative thoracic radiotherapy in non-small cell lung cancer. An analysis of 1250 patients. Palliation of symptoms, tolerance and toxicity. Lung Cancer. 2011;71:344-9.
13. Sau S, Sau S, Dutta P, Gayen GC, Banerjee S, Basu A. A comparative study of different dose fractionations schedule of thoracic radiotherapy for pain palliation and health-related quality of life in metastatic NSCLC. Lung India : Official Organ of Indian Chest Society. 2014;31:348-53.
14. Wang J, Xia TY, Wang YJ, Li HQ, Li P, Wang JD, et al. Prospective study of epidermal growth factor receptor tyrosine kinase inhibitors concurrent with individualized radiotherapy for patients with locally advanced or metastatic non-small-cell lung cancer. Int J Radiat Oncol Biol Phys. 2011;81:59-65.
15. Laporte S, Squifflet P, Baroux N, Fossella F, Georgoulias V, Pujol J, et al. Prediction of survival benefits from progression-free survival benefits in advanced non-small-cell lung cancer: evidence from a meta-analysis of 2334 patients from 5 randomised trials. BMJ Open. 2013;3(3):e001802.
16. Imperatori A, La Salvia D, Rotolo N, Nardecchia E, Bandera M, Toungoussova O, et al. Five-year survival of stage IIIA-IIIB (non-N3) non-small cell lung cancer patients after platinum/gemcitabine induction chemotherapy and surgery. J Chemother. 2010;22:191-6.
17. Dharma-Werdene M, Au HJ, Hanson J, Dupere D, Hewitt J, Feeny D. Baseline FACT-G score is a predictor of survival for advanced lung cancer. Qual Life Res. 2004;13:1209-16.

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