

The clinicopathological profile and treatment outcomes of stage IV lung cancer patients treated at a tertiary cancer center in India

Gunjan Shrivastav^{1*}, Sandeep Batra², Nitesh Rohatgi³, Alok Gupta⁴, Hiba Siddiqui²,
Devavrat Arya², Ankur Bahl³, Harit Chaturvedi²

¹Department of Oncology, Cancer Hospital and Research Institute, Gwalior, Madhya Pradesh, India

²Department of Oncology, Max Super Speciality Hospital, Saket Institutional Area, Saket, New Delhi, India

³Department of Oncology, Fortis Memorial Research Institute, Gurugram, Haryana, India

⁴Department of Medical Oncology, Medanta Hospital, Lucknow, Uttar Pradesh, India

Received: 20 May 2024

Revised: 04 July 2024

Accepted: 17 October 2024

*Correspondence:

Dr. Gunjan Shrivastav,

E-mail: gunjan.shrivastav23@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Non-small cell lung cancer (NSCLC) is a devastating disease that originates from a complex combination of genetic, environmental, and lifestyle factors. A prospective study was conducted at Max Hospital, Saket, New Delhi, to assess the above factors in stage IV lung cancer patients and determine the survival rate and quality of life (QOL) parameters post-administration of the recommended first-line therapy.

Methods: The primary objective of the study was to determine progression-free survival (PFS) in stage IV lung cancer patients after receiving the first-line therapy. This study also evaluated the clinical and histopathological profile of patients, survival rate, and QOL parameters after the administration of first-line therapy, which includes chemotherapy, tyrosine kinase inhibitors (TKI), immunotherapy, and chemo-immunotherapy.

Results: The study enrolled 85 patients (63 males, 22 females) with a mean age of 64.08 ± 10.3 years. The median PFS was 10.56 months, with a six-month survival rate of 74.3% and a one-year overall survival rate of 58.3%. Among stage IV lung cancer patients, adenocarcinoma was more common (64.71%), especially in females (86.36%) compared to males (57.14%). Out of 85 patients, 54 completed the QOL questionnaire at baseline and follow-up, showing significant improvement in QOL scores during follow-up ($p < 0.0001$).

Conclusions: This prospective study showed improvement in PFS compared to the studies already conducted in different parts of India. A notable trend of increase in NSCLC was observed among females. Improvement in QOL scores was observed in patients who received chemotherapy and TKI as the first-line therapy.

Keywords: Chemotherapy, Lung cancer, Progression-free survival, Quality of life, Tyrosine kinase inhibitors

INTRODUCTION

Cancer is a formidable foe that continuously challenges the boundaries of medical science and human endurance, making it a leading cause of death, accounting for 10 million deaths in 2020, as per WHO.¹ Among its many forms, lung cancer is the most diagnosed and lethal malignancy, responsible for 18% of the total cancer deaths. In 2020, there were 2.2 million new cases of lung cancer reported by GLOBOCAN worldwide, causing 1.7 million deaths.² Recent data from the India's National

Cancer Registry Program, it is the topmost cancer diagnosed in males and is expected to be the fifth most common cancer in females by 2025. The most recent estimates for cancer in India have increased by five percent (from 13, 92, 179 in 2020 to 14, 61, 427 in 2022).^{3,4}

Due to its ambiguous presentation, lack of a regular screening strategy, and frequent misdiagnosis as tuberculosis in our nation, lung cancer is often diagnosed at an advanced stage.⁵ Also, the recent shift observed in

the incidence of lung cancer among women may be linked to targetable mutations and cannot be solely attributed to the increase in smoking habits within this demographic.^{5,6} Furthermore, adenocarcinoma has overtaken squamous cell carcinoma (SCC) as the most prevalent histological subtype of non-small cell lung cancer (NSCLC) in India.⁷

With a better and deeper understanding of the molecular pathways involved in cancer development, advancement in diagnostic techniques, and the development of new therapeutic approaches such as targeted therapy and immunotherapy, the survival rates of patients with lung cancer have increased significantly. The diagnosis of lung cancer has also evolved beyond histological and immunohistochemical examinations, focusing on identifying the presence of oncogenic driver mutations and immunotherapy efficacy markers.⁸ The National Comprehensive Cancer Network (NCCN) recommends testing for various genetic alterations in all locally advanced or metastatic NSCLC patients, allowing for tailored treatments with mutation-directed tyrosine kinase inhibitors (TKIs).⁹

Third-generation TKIs like Osimertinib and second-generation TKI, Alectinib, demonstrated improved progression-free survival (PFS) in EGFR-mutated and ALK-rearranged NSCLC, respectively.^{10,11} Immunotherapy has also brought significant advancements, particularly with Programme Death receptor (PD1) inhibitors and PDL1 inhibitors yet predicting the patient population that shows maximum benefit remains a challenge.¹² While the available treatment like TKI, immunotherapy and chemotherapy offers symptom relief and improved survival, variable impact on patient's quality of life (QOL) should be considered crucially. Therefore, balancing disease management, treatment side effects, expected benefits, and QOL remains essential in the comprehensive care of lung cancer patients amid rapid changes in the clinicopathological and treatment profile.^{13,14}

Thus, the present study was conducted to assess the abovementioned factors in stage IV lung cancer patients with the goal of gaining a deeper insight into their clinical profiles and survival rates after the administration of first-line therapy. Such insights would assist us in studying their QOL parameters and would further help in formulating improved care strategies for the future.

METHODS

Study design

This was a prospective, observational, and descriptive study conducted at the Max Super Specialty Hospital, Saket, New Delhi. The study was conducted for a period of 1.2 years between 1st June 2019 and 30th August 2020. Since it was an observational study, it did not involve any modification in the ongoing patient treatment plan.

Patients' history was collected after their consent, along with clinical data from hospital records, including case files and hospital software, namely CPRS, e-prescription, and discharge summaries, to determine our objectives. The protocol was reviewed and approved by the ethics committee responsible for the oversight of the study. This research was carried out in accordance with the basic principles defined by ICMR's ethical guidelines for biomedical research on human participation (2006), and CDSO guidelines on good clinical practice for clinical research in India. Patients were identified only by a participant identification number (patient ID) to maintain confidentiality.

Patient disposition and treatment

The study recorded the demographic profile of the patients in detail, including age, gender, and address. It included newly diagnosed and histopathologically confirmed cases falling into the stage IV NSCLC category as per the American Joint Commission on Cancer (AJCC) 8th edition criteria.¹⁵ Patients who received treatment (systemic chemotherapy, targeted therapy, and/or immunotherapy) at our center, relapsed after surgery or definitive chemoradiation, and patients unfit for systemic therapy for stage IV NSCLC were included. Smoking history, including the duration and form of smoking and other types of tobacco intake, was recorded. Never smokers were defined as individuals who have consumed <100 cigarettes/beedis in their lifetime, while ever smokers were defined as those who had smoked 100 cigarettes/beedis in their lifetime. Foreign nationals, patients seeking opinion, and individuals having SCLC or other malignancies were excluded from the study.

Diagnosis of stage IV NSCLC patients

Patients were subjected to basic hematological, radiological, and microbiological investigations. Tissue specimens were further subjected to immunohistochemical staining for classification into histological subtypes based on the recent WHO classification. Individuals with positive IHC staining for CK7, TTF1, and Napsin A were diagnosed with adenocarcinoma, while CK5/6 and p63-positive patients were diagnosed with squamous cell carcinoma. TaqMan-based real-time PCR was used for the detection of EGFR mutation, and EML4-ALK mutations were detected by immunohistochemistry (IHC) or fluorescence in-situ hybridization (FISH) as applicable. ROS1 gene rearrangement was also tested by FISH as applicable.

Treatment

Patients received treatment at the discretion of the treating physician and were informed of the decision. They were subjected to clinical evaluation by history and examination at each hospital visit. Response assessment was done by CECT chest or PET-CT based on the initial

investigation done and the current situation. Responses were then coded as per the response evaluation criteria in solid tumors (RECIST) criteria 1.1 (75). In case of suspected disease progression at any point of therapy, radiological reassessment was done. Patients with 1st line treatment failure or disease progression after first-line therapy were offered second-line treatment or best supportive care as per their fitness level. PFS was calculated from the date of initiation of treatment to the date of disease progression or death. Overall survival (OS) was calculated from the date of initiation of treatment to the date of last follow-up or death. For survival analysis, all patients were censored at the last date of follow-up.

Study outcomes

The study was conducted to determine the clinicopathological profile and treatment outcomes of stage IV lung cancer patients. The primary endpoint was to determine PFS on first-line therapy. The secondary endpoints were to measure the clinical and pathological profile of stage IV cancer patients along with the response rate and survival rate after the administration of first-line therapy. The clinical profile includes performance status, smoking history, and presence or absence of co-morbidities, while the pathological profile determines the histopathological and molecular subtype (EGFR, ALK, and ROS 1 mutation) of stage IV NSCLC patients. The QOL was assessed by the European Organization for Research and Treatment of Cancer Core Quality of Life (EORTC-QOL-C30) questionnaire which was made available in both English and Hindi language.

Statistical analysis

The data collected was analyzed using SPSS version 20. Study data was presented as descriptive data. Age, gender and pathological type were analyzed by calculating percentages. The score of QOL before and after therapy was presented as mean (standard deviation), and the difference was calculated using the student’s t-test. Kaplan Meir curves were used to assess OS and PFS. Partial response rate and complete response rate were calculated along with 85% confidence intervals. Statistical significance was considered at p<0.05.

RESULTS

Patients’ demographics

A total of 85 patients willingly participated in the study between June 2019 and August 2020. The median age of the study population was 63 years, with 29.41% of patients below 60 years of age, 65.88% of patients aged between 60-80 years, and 4.71% of patients above 80 years of age. The male population predominated with a male-to-female ratio of 2.86. Females had a lower median

age (60.5 years) as compared to males (66 years), and this difference was statistically significant (p<0.05).

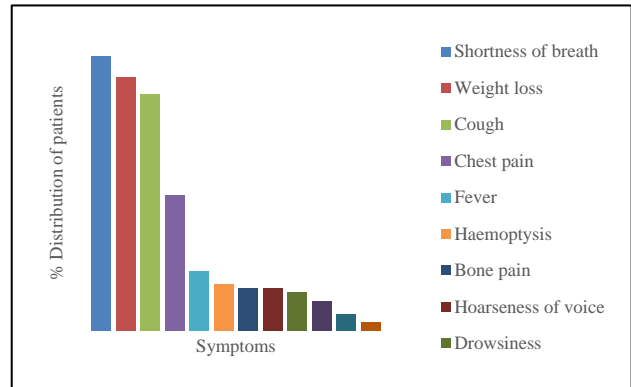


Figure 1: Percentage distribution of symptomatic patients.

Only a small fraction of patients (10 out of 85) was incidentally diagnosed without any symptoms, while 75 patients had symptoms on presentation. The top five symptoms reported were shortness of breath, weight loss, cough, chest pain, and hemoptysis. Figure 1 shows the percentage distribution of symptomatic patients during presentation.

Most patients (84.70%) were newly diagnosed with metastatic disease, while 15.3% patients had developed metastatic disease at recurrence or progression after receiving treatment for localized disease.

Modality of diagnosis

The primary diagnosis was confirmed through biopsy in 65.88% of patients, FNAC in 30.58% of patients, pleural fluid analysis in 2.35%, and pericardial fluid analysis in 1.18% of patients. The primary site was the most commonly biopsied (69.41%) followed by lymph node (17.64%), bone (5.88%), and liver (4.70%). Additionally, one patient had a brain biopsy, and the other had an adrenal glands biopsy comprising 2.35% of the total site biopsied. PET CT was done for 95.29% of study participants and MRI brain was done for 41.17% of patients. The patient-wise distribution of the clinical stages T, N, and M are reported in Table 1.

Treatment

First line therapy

Out of total study population, 18 patients were either defaulted on or considered unfit for any systemic therapy. Among the remaining patients, 35 underwent chemotherapy, 5 received immunotherapy, 3 were given chemoimmune therapy, 23 received TKI therapy, and 1 patient received a combination of chemotherapy and TKI therapy (Table 2).

Table 1: Demographic and baseline characteristics of patients.

Variables	Subgroup	Value (N, %)	
Age (years) (n=85)	≤60	25, 29.41	
	60-80	56, 65.88	
	≥80	4, 4.71	
	Median age (IQR)	63 (58-73)	
	Mean age (±SD)	64.08±10.03	
Gender	Male	63, 74.11	
	Female	22, 25.89	
BMI (Mean±SD)		23.42±4.77 kg/m ²	
Smoking status	Never smokers	37, 43.52	
	Ever smokers	48, 56.48	
Presentation mode	Incidental	10, 11.76	
	Symptomatic	75, 88.24	
ECOG status	1	5, 5.88	
	2	34, 40	
	3	33, 38.82	
	4	13, 15.30	
TNM staging	T stage	T2	8, 9.42
		T3	23, 27.05
		T4	50, 58.82
		Tx	4, 4.71
	N stage	1	1, 1.17
		2	19, 22.35
		3	65, 76.47
	M stage	Brain metastasis	22, 25.88
		Bone metastasis	48, 56.47
		Lung metastasis	32, 37.64
Liver metastasis		19, 22.35	

IQR: inter quartile range; BMI: body mass index; SD: standard deviation; TNM: tumor, node, and metastases.

Table 2: The detailed distribution of the above therapies received by 67 patients.

Therapies prescribed	Number of patients	
TKI	Alectinib	2
	Crizotinib	3
	Erlotinib	11
	Gefitinib	4
	Osimertinib	4
Immunotherapy	Atezolizumab	3
	Pembrolizumab	4
	Nivolumab	1
Chemotherapy	Pemetrexed/platinum	15
	Taxane/platinum	16
	Pemetrexed monotherapy	1
Chemo-immunotherapy	Bevacizumab + pemetrexed/ platinum	3
Total number of patients	67	

TKI: Tyrosine kinase inhibitor

Radiotherapy was administered to 45 patients, with 35 patients receiving it as part of their initial treatment, 4 patients received it during their first-line therapy, and 6 patients upon disease progression. The most frequent site for radiotherapy was the brain, followed by the bones and the primary lesion.

Overall, Table 3 shows the administration of first-line therapy based on the histopathological grades of carcinoma. It was observed that a higher proportion of adenocarcinoma (9.1%) were eligible for immunotherapy compared to squamous cell carcinoma (8.33%), but this difference was not statistically significant (p value =0.9339).

Table 3: Administration of first-line therapy on the basis of histopathological grades.

Histo-grade	Defaulted	Chemo therapy	Immuno therapy	Chemo immunotherapy	TKI therapy	Chemo plus TKI	Overall
Adenocarcinoma	15	15	2	3	19	1	55
Squamous cell carcinoma	2	9	1	0	0	0	12
Adeno-squamous carcinoma	1	8	2	0	2	0	13
Poorly differentiated	0	2	0	0	2	0	4
Large cell carcinoma	0	1	0	0	0	0	1
Grand total	18	35	5	3	23	1	85

Second line therapy

On the progression of the disease, 25 patients (29.41%) out of the entire study population went on to receive second-line therapy that consisted of TKI, immunotherapy, chemotherapy, chemoimmunotherapy, and chemotherapy in combination with TKI. Figure 2 below shows the patient-wise distribution of second-line therapy.

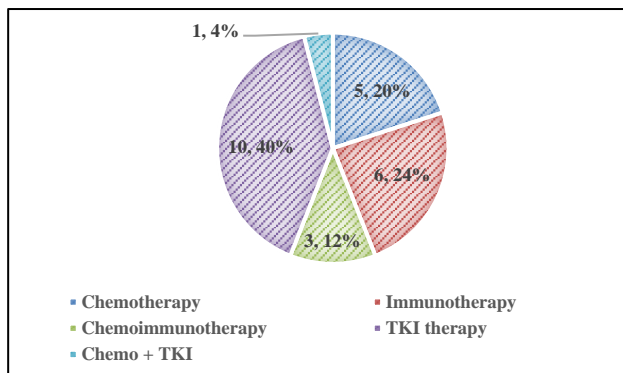


Figure 2: Percentage of patients treated with second line therapy.

Outcomes

Primary outcomes

The primary endpoint was to determine the PFS on the first line therapy. The six-month PFS was 65.5%, and the one-year PFS was 46.8%. The median PFS for the entire population was 10.56 months. Median PFS differed amongst the different treatment modalities. The highest PFS was seen with TKI therapy (10.67 months) followed by chemotherapy (8.604 months). The PFS was undefined in immunotherapy and a combination of chemotherapy plus TKI arm due to the smaller study size. Although numerical differences were present between TKI and chemotherapy arms, they did not reach statistical significance (Figure 3).

Secondary outcomes

The secondary endpoint of the study was to determine the clinical and pathological profile of patients receiving

first-line therapy, followed by assessing the response rate, survival rate, and QOL parameters of the cancer patients.

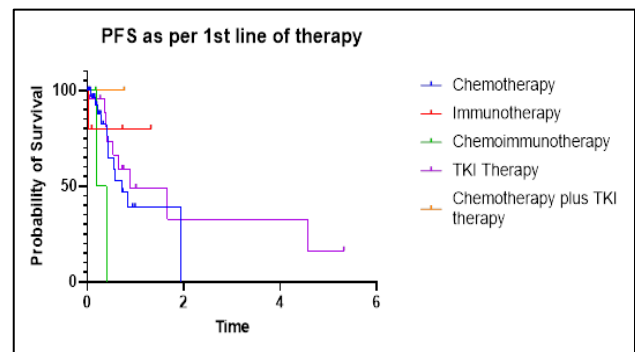


Figure 3: Progression free survival (PFS) after the administration of first line therapy (p<0.05).

Clinical profile

Of the total study population, more than half of the patients (55.3%) had one or more co-morbidities, with diabetes mellitus, hypertension, COPD, coronary artery disease, and hypothyroidism being the top five co-morbidities (Figure 4).

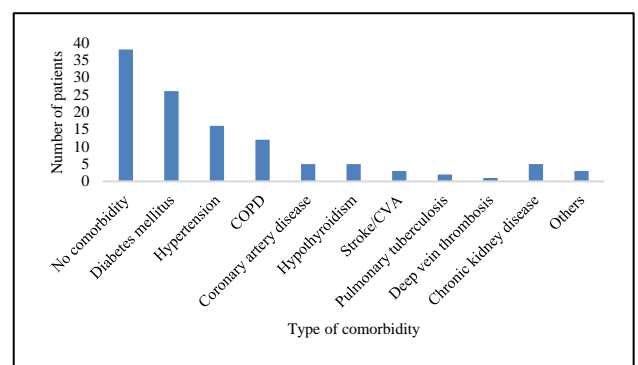


Figure 4: Distribution of patients having comorbidity on presentation (n=85).

With reference to Eastern Cooperative Oncology Group performance status (ECOG PS) score, the study population had 5.88% patients with grade ECOG PS 1, 40% patients with ECOG PS 2, 38.82% patients with ECOG PS 3 and 15.30% patients with ECOG PS 4. The

smoking history of the patients revealed that 56.48% individuals were ever-smokers and 43.52% were never-smokers (Table 1).

Pathological profile

The histopathological examination revealed that adenocarcinoma was the most common subtype of cancer, accounting for 64.71% of cases, followed by adenosquamous carcinoma in 15.29% of patients, squamous cell carcinoma in 14.11%, poorly differentiated carcinoma in 4.70% and large cell carcinoma in 1.17% patients. The gender-wise distribution of type of carcinoma examined via histopathological analysis revealed that a higher proportion of females (86.36%) had adenocarcinomas compared to males (57.14%), but this difference was not statistically significant.

In all 60 out of 85 patients tested for EGFR and ALK mutations, 24 patients (40%) tested positive for EGFR, and 6 patients (9.7%) were diagnosed with ALK mutations. Exon 19 deletion (16 patients) was the most common mutation seen in EGFR analysis, exon 21 L858R mutation was seen in 7 patients, and 1 patient had exon 20 insertion mutation. Out of six ALK mutated patients, four were IHC positive, while 2 were FISH positive. All 59 patients were tested negative for ROS1 mutation. Amongst the patients tested for PDL1, the score was negative (PDL1<1%) in 6 patients, positive in 19 patients, with a value between 1- 50% in 7, and >50% in 7 patients.

Response assessment

The overall response assessment was not possible for all the patients involved in the study as some patients were assigned to best supportive care, a few were defaulted, and one had early clinical deterioration. Complete radiological response to first-line therapy was seen in three patients, partial response in 21 patients, and stable disease in seven patients. Progressive disease was seen in nine patients on the first follow-up scan.

Among the three patients who achieved a complete response, one received immunotherapy, while two were treated with TKI therapy. Among the 21 patients who had a partial response, 15 underwent chemotherapy, five received TKI monotherapy, and one patient received a combination of TKI and chemotherapy. Among the seven patients with stable disease, three were treated with TKI monotherapy, two received immunotherapy, and two were administered chemotherapy.

Response assessment post-initiation of second-line therapy was done in 13 out of 25 patients who showed progression of the disease. Out of 13, one had complete response, two had partial response, six had stable disease, and four had progressive disease (Figure 5).

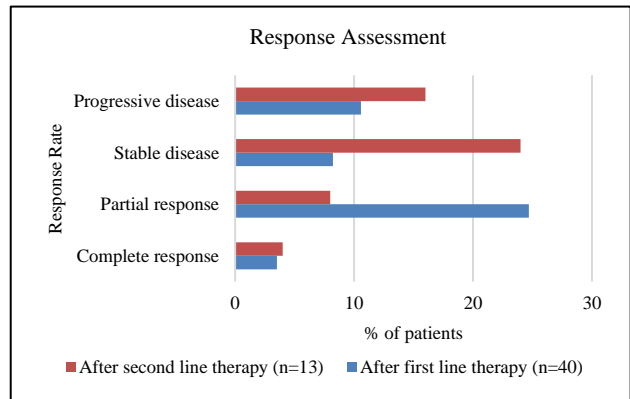


Figure 5: Response assessment after the administration of first-line therapy and second line of therapy.

Survival rate

At the end of the study, 62 patients had died, and 23 were alive. The six-month survival rate was 74.3%, and the one-year overall survival rate was 58.3%. The median overall survival was undefined due to the study’s relatively small sample size (Figure 6, Table 4).

Table 4: Distribution of overall survival rate as per the type of first line of therapy (p<0.05) and the histopathology grade.

Category/therapy	Median survival (months)	6-month PFS (%)	12-month PFS (%)
Chemotherapy	8.796	72.90	43.70
Immunotherapy	Undefined	80	80
Chemoimmunotherapy	Undefined	100	100
TKI Therapy	Undefined	82.90	82.90
Chemo plus TKI therapy	Undefined	100	100
Histopathology grade			
Adenocarcinoma	Undefined	72.40	63.40
Squamous	Undefined	64.80	64.80
Adeno-squamous	Undefined	90.90	64.90
Poorly differentiated	0.733744	100	0
Large cell carcinoma	0.15332	0	0

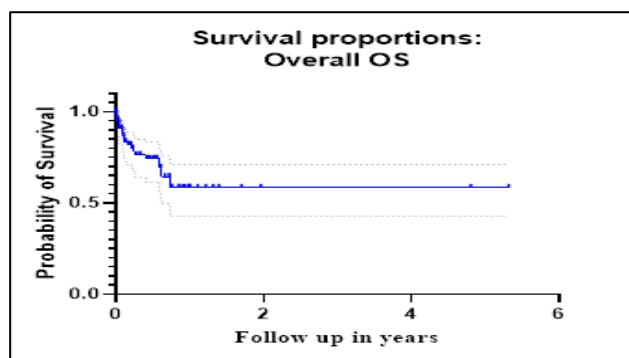


Figure 6: Graph representing overall survival rate.

QOL

Not all patients who consented to the study filled up the QOL questionnaire due to reasons such as early deterioration, sick patients going to the critical care unit at presentation, attendants not disclosing diagnosis, or personal preference. Of the total 85, baseline and follow-up questionnaires were filled out by 54 patients. Of these, the majority were those who received chemotherapy in the first-line setting (48.14%), followed by TKI (with or without chemotherapy in 31.47% of patients, and immunotherapy (with or without chemotherapy in 14.8%). Overall, the QOL parameters showed a significant improvement in the scores during the follow-up of the patients compared to the baseline ($p < 0.0001$). The QOL parameters comprising physical, emotional, cognitive, and social functioning were improved on follow-up after the treatment; this improvement was significantly different ($p < 0.0001$). The questionnaire also exhibited that symptoms at the time of the presentation were decreased significantly ($p < 0.0001$), improving the QOL.

DISCUSSION

This prospective study conducted at Max Hospital, Saket, New Delhi, included stage IV lung cancer patients to determine their PFS after the treatment with first line therapy and recorded the survival rate of the patients and the difference in the QOL parameters after the treatment.

The median age of our study population was 63 years which was notably higher than the ages reported in previous studies.^{7,16} Moreover, there was an increased number of female patients suffering from NSCLC (25.89%) potentially influenced by the inclusion of patients from rural areas, indicating referral bias. This led to the male-to-female ratio of 2.86, lower than the earlier reported range (3.2-4.6).

Until recent times, NSCLC was associated with individuals who were ever smokers, but lately, a notable increase among non-smokers has been witnessed. Nearly half of the participants in our study (43.52%) were never

smokers, which is greater than the percentage reported by Malik et al (32.16%) but close to that of Murali et al (46.6%).^{7,15} This emphasizes how crucial it is to keep a healthy dose of caution when assessing individuals exhibiting symptoms. The majority of our patients (88.24%) had symptoms when they arrived, and a sizable number (84.70%) had reached stage IV. Notably, only about 10% of the total population were presented with warning signs like hoarseness of voice, hemoptysis, bone pain, and seizures.

Our results demonstrated a notable difference in the median PFS (10.56 months), surpassing the usual range of six to eight months.¹⁷ This PFS was also higher than the median PFS (5.7 months) reported by Murali et al 2017.⁷ It was also observed that patients receiving TKIs showed better PFS compared to those who received chemotherapy alone (8.604 months). So, the increase in overall PFS can be attributed to the increase in TKI use in the first-line scenario. These findings are in line with PFS results seen in clinical trials covering the majority of first-generation TKIs.^{18,19} The extended tail of the Kaplan-Meier curve shows that few TKI-treated patients continued to respond throughout the study. Notably, two patients with initial diagnoses in 2015 who sought medical attention at our center both tested positive for EGFR mutations and were still alive at the study's completion. The non-significant difference amongst various treatment modalities could be due to a smaller study size. The median PFS on second-line therapy was only 4.17 months, underlining the importance of using the best available treatment in the first line as many patients may never be able to receive second-line therapy.

Our study revealed a higher percentage of adenocarcinomas (64.71%), exceeding the numbers reported by Malik et al (45.41%) and Murali et al (51.1%).^{7,16} Notably, the EGFR mutation rate (40%) in our study was greater than that of other studies, which found that 20-30% of Indian patients had EGFR mutations.²⁰ The elevated EGFR mutation rate in our research may be attributed to the larger proportion of adenocarcinomas and female patients. Additionally, the percentage of ALK mutations in our study (9.7%) is consistent with earlier research from our institute conducted by Singh et al a multicenter study by Doval et al.^{21,22} In contrast, none of our patients exhibited ROS1 mutations, indicating that this mutation is less prevalent.

The increased effect of TKIs and the higher percentage of patients with driver mutation-positive status highlight the significance of early mutation testing and proper therapy, yet challenges prevail. Cost restrictions and insufficient tissue for mutation analysis are major problems in our country. Despite a total mutation-positive rate of 35.3%, only 28.22% of patients in our research received tyrosine kinase inhibitors in the first-line context. This disparity is because of several factors, such as a greater disease burden, a delay in receiving mutation data, and TKI

affordability. Osimertinib was recently approved for first-line NSCLC treatment. However, due to its high cost, only one-third of EGFR mutation-positive patients received it in the first line, limiting its curative potential. Similarly, 16.47% of patients tested positive for PDL1 score, but only 9.4% received immunotherapy in a first-line setting, highlighting the lack of access to expensive medications in the clinical setup.

Even though overall survival is the gold standard for assessing the efficacy of any treatment, determining QOL is a crucial parameter for treating stage IV cancer where palliative care is the primary objective. Our study showed a significant improvement in all the QOL parameters ($p < 0.0001$), yet the small sample size of patients receiving immunotherapy, the financial burden due to the center being corporate set up, and substantial portions of patients unfit for systemic therapy were the limitations of the study. Though insurance and aid from the government helped many but, it was not true for all the patients undergoing treatment.

CONCLUSION

Lung cancer is a deadly disease, but with new developments, we may be able to offer better hope to our patients. The elderly population and the presence of comorbidities can mask common symptoms and lead to delayed diagnosis. In our country, tuberculosis remains a significant disease that can mimic lung cancer, reflecting the lack of an effective screening program and low awareness among physicians regarding the early evaluation of suggestive symptoms. A lung cancer registry program detailing the profile and performance of Indian patients would be welcome in order to make guidelines more suitable for our patient population.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of Max Superspeciality Hospital (A Unit of Devki Devi Foundation), New Delhi

REFERENCES

- World Health Organization. Cancer. 2023. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>. Accessed on 26 September 2023.
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-49.
- Sathishkumar K, Chaturvedi M, Das P, Stephen S, Mathur P. Cancer incidence estimates for 2022 & projection for 2025: Result from National Cancer Registry Programme, India. *Indian J Med Res*. 2022;156(4 and 5):598-607.
- Mathur P, Sathishkumar K, Chaturvedi M, Das P, Sudarshan KL, Santhappan S, Nallasamy V, John A, Narasimhan S, Roselind FS, Icmr-Ncdir-Ncrp Investigator Group. Cancer statistics, 2020: report from national cancer registry programme, India. *JCO Glob Oncol*. 2020;6:1063-75.
- Noronha V, Dikshit R, Raut N, Pramesh CS, Karimundackal G, Agarwal JP, et al. Epidemiology of lung cancer in India: focus on the differences between non-smokers and smokers: a single-centre experience. *Indian J Cancer*. 2012;49(1):74-81.
- Mohan A, Garg A, Gupta A, Sahu S, Choudhari C, Vashistha V, et al. Clinical profile of lung cancer in North India: A 10-year analysis of 1862 patients from a tertiary care center. *Lung India*. 2020;37(3):190-7.
- Murali AN, Radhakrishnan V, Ganesan TS, Rajendranath R, Ganesan P, Selvaluxmy G, et al. Outcomes in lung cancer: 9-year experience from a tertiary cancer center in India. *J Glob Oncol*. 2017;3(5):459-68.
- Howlader N, Forjaz G, Mooradian MJ, Meza R, Kong CY, Cronin KA, et al. The effect of advances in lung-cancer treatment on population mortality. *N Engl J Med*. 2020;383(7):640-9.
- National Comprehensive Cancer Network. version 1.2024. 2023. NSCLC. Available from: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed on 27 September 2023.
- Soria JC, Ohe Y, Vansteenkiste J, Reungwetwattana T, Chewaskulyong B, Lee KH, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. *N Engl J Med*. 2018;378(2):113-25.
- Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer. *N Engl J Med*. 2017;377(9):829-38.
- Doroshov DB, Sanmamed MF, Hastings K, Politi K, Rimm DL, Chen L, et al. Immunotherapy in non-small cell lung cancer: facts and hopes. *Clin Cancer Res*. 2019;25(15):4592-602.
- Mannion E, Gilmartin JJ, Donnellan P, Keane M, Waldron D. Effect of chemotherapy on quality of life in patients with non-small cell lung cancer. *Support Care Cancer*. 2014;22(5):1417-28.
- Ramirez RA, Lu J, Thomas KEH. Quality of life for non-small cell lung cancer patients in the age of immunotherapy. Vol. 7, *Translational Lung Cancer Research*. AME Publishing Company; 2018:S149-S152.
- Keung EZ, Gershenwald JE. The eighth edition American Joint Committee on Cancer (AJCC) melanoma staging system: implications for melanoma treatment and care. *Exp Rev Anticancer Ther*. 2018;18(8):775-84.
- Malik PS, Sharma MC, Mohanti BK, Shukla NK, Deo SVS, Mohan A, et al. Clinico-pathological profile of lung cancer at AIIMS: a changing paradigm in India. *Asian Pac J Cancer Prevent*. 2013;14(1):489-94.

17. Rajappa S, Gundeti S, Talluri M, Digumarti R. Chemotherapy for advanced lung cancer: a 5-year experience. *Indian J Cancer.* 2008;45(1):20.
18. Mitsudomi T, Morita S, Yatabe Y, Negoro S, Okamoto I, Tsurutani J, et al. Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial. *Lancet Oncol.* 2010;11(2):121-8.
19. Rosell R, Carcereny E, Gervais R, Vergnenegre A, Massuti B, Felip E, et al. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol.* 2012;13(3):239-46.
20. Shi Y, Au JSK, Thongprasert S, Srinivasan S, Tsai CM, Khoa MT, et al. A prospective, molecular epidemiology study of EGFR mutations in Asian patients with advanced non-small-cell lung cancer of adenocarcinoma histology (PIONEER). *J Thorac Oncol.* 2014;9(2):154-62.
21. Singh R, Rohtagi N. Clinicopathological and molecular epidemiological study of lung cancer patients seen at a tertiary care hospital in northern India. *South Asian J Cancer.* 2017;06(04):171-5.
22. Doval D, Prabhash K, Patil S, Chaturvedi H, Goswami C, Vaid A, et al. Clinical and epidemiological study of EGFR mutations and EML4-ALK fusion genes among Indian patients with adenocarcinoma of the lung. *Onco Targets Ther.* 2015;117.

Cite this article as: Shrivastav G, Batra S, Rohatgi N, Gupta A, Siddiqui H, Arya D, et al. The clinicopathological profile and treatment outcomes of stage IV lung cancer patients treated at a tertiary cancer center in India. *Int J Res Med Sci* 2024;12:4091-9.