Original Article

The Impact of Medication Adherence on Total Treatment Costs in Patients with Non-Small Cell Lung Carcinoma

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Abstract

Background: Lung cancer is the leading cause of cancer-related death globally and ranks second in cancer incidence in Indonesia. Targeted therapies such as Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitors (EGFR-TKIs) and Anaplastic Lymphoma Kinase (ALK) inhibitors are recommended for advanced-stage non-small cell lung cancer (NSCLC) but may be limited by high cost. This study aimed to assess the relationship between medication adherence—measured by the mean proportion ratio (MPR)—and total treatment costs, and to examine its association with patient-specific factors.

Methods: This observational, cross-sectional study used secondary data from NSCLC patients treated with EGFR-TKIs or ALK inhibitors at a Cancer Center in Jakarta, Indonesia (January 2023-March 2025). Eighty-six eligible patients (aged ≥18 years) were diagnosed with NSCLC, confirmed by immunohistochemistry (EGFR or ALK-positive). MPR measured medication adherence and analysed using Mann-Whitney and chi-square tests using SPSS Version 23, with a value of $P<0.05$ being significant.

Results: Among NSCLC patients, about 89.53% exhibited a high level of treatment adherence, with an MPR score ≥0.8. Most patients were female (62.8%), under 60 years old (51.2%), stage IV (74.4%), and had an EGFR exon 19 mutation (52.3%). Osimertinib (30.2%) and Afatinib (24.4%) were the most used therapies. Most patients reported no serious side effects (57.0%) and received caregiver support (57.0%). There was no significant association between medication adherence and treatment cost ($P=0.955$), nor patient-related factors.

Conclusion: Approximately 9 out of 10 NSCLC patients adhere to treatment with EGFR-TKIs or ALK inhibitors. High levels of adherence did not significantly increase additional medical expenses that would raise the total cost of treatment. Further qualitative research is needed to explore adherence determinants.

Keywords: adherence, NSCLC, targeted therapy, total treatment cost

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INTRODUCTION

According to World Health Organization (WHO) data, lung cancer is the most prevalent cancer globally, with 2.5 million cases (12.4% of all cancers globally) and the leading cause of cancer-related deaths.[1] In Indonesia, it ranks second (9.5% of all cancer cases) after breast cancer (16.2% of all cancer cases), and is more common among male patients with a history of smoking.[2,3] Non-small cell lung cancer (NSCLC) is the most common type, accounting for 85% of lung cancer cases. In the Asian population, Epidermal Growth Factor Receptor (EGFR) mutations represent the most prevalent genetic alteration among NSCLC patients (40–55%), followed by Anaplastic Lymphoma Kinase (ALK) mutations (3–9%).[4,5]

Targeted therapy is one of medications for lung cancer that works by blocks specific molecules or pathways involved in cancer cell growth and progression while minimizing damage to normal cells. Oral targeted therapy is recommended as it reduces the side effects of invasive chemotherapy, such as phlebitis, and eliminates the need for hospitalization.[6] The Indonesian Lung Cancer Guidelines also recommend targeted therapy for advanced-stage NSCLC, including oral agents such as Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitors (EGFR-TKIs) and ALK inhibitors.[7]

While targeted therapy aligns with the principles of precision medicine, its high-cost limits accessibility. Oral targeted therapy allows patients to self-administer

their medication at home. However, because the treatment is administered independently, healthcare professionals cannot monitor patients' adherence to direct therapy. Patients' nonadherence to targeted therapy will affect its efficacy and increase treatment costs due to disease progression.[8] Adherence itself is influenced by factors such as age, polypharmacy, adverse effects, understanding of treatment, access, and caregiver support.[7–9]

Adherence is commonly assessed using the mean proportion ratio (MPR), which compares the amount of medication obtained to the total prescribed duration. An MPR ≥0.8 indicates adherence, while <0.8 denotes non-adherence.[10] This MPR evaluation requires a minimum of 3 months of therapy.[11] Therefore, this study will assess the relationship between adherence, specifically EGFR-TKIs or ALK inhibitors and total treatment costs and total treatment costs and examine their association with patient-specific factors.

METHODS

This research employed an observational approach utilizing a cross-sectional study design. Data were collected from secondary sources, including patient medical records from the Department of Medical Records at the Cancer Center in Jakarta, Indonesia. The study population consisted of individuals diagnosed with NSCLC who received EGFR-TKIs or ALK inhibitors between January 2023 and March 2025. The EGFR-TKIs drugs used in this study included Gefitinib, Erlotinib, Afatinib, and Osimertinib, whereas the ALK Inhibitors used were Alectinib, Crizotinib, and Lorlatinib.

The inclusion criteria for this study were patients aged at least 18 years diagnosed with NSCLC, with immunohistochemistry results of EGFR or ALK positive. The exclusion criteria in this study were incomplete patient medical records, patients who did not receive targeted therapy due to national drug shortages, targeted therapy was changed to other agents besides EGFR-TKI or ALK inhibitors based on the doctor's recommendations, and patients did not receive drugs from this hospital.

Adherence to targeted therapy was measured using the MPR, defined as the number of days the medication was received divided by the total prescribed duration, from January 2023 to March 2025. Meanwhile, the total medical costs in this study were categorized into three components: direct medical costs, indirect medical costs, and opportunity costs. The total medical costs were calculated over the period during which patients received EGFR-TKIs or ALK inhibitors.

Direct medical costs comprised expenses related to targeted therapy, physician consultations, supportive medications, hospitalization, laboratory examinations, radiological procedures, diagnostic services, and surgical interventions. Indirect medical costs included transportation expenses incurred for travel between the patient’s residence and the hospital, as well as caregiver costs for respondents who utilized non-family caregiver services. Opportunity costs were defined as the loss of productive time resulting from hospital visits for physician consultations and the collection of targeted therapy medications.

Data were analysed using the Mann-Whitney and chi-square tests in SPSS version 23, with a significance level of $P<0.05$. Ethical approval was granted by the Universitas Indonesia Hospital Ethics Committee (No. S-060/ KETLIT/RSUI/II/2025).

RESULTS

A total of 86 patients were included in this study. Based on the sociodemographic characteristics presented in Table 1, females (62.8%), non-geriatric patients or aged <60 years (51.2%) and non-smokers (54.7%) constituted the majority of the NSCLC population. Most patients were diagnosed with stage IV NSCLC (74.4%) and received fewer than five types of medications (59.3%). Meanwhile, in Table 2, some of these patients had multiple types of metastases, with bone (32.67%) and brain (21.78%) metastases being the most common among NSCLC patients. The immunochemistry results in NSCLC patients showed EGFR exon 19 (52.3%) and EGFR exon 21 (26.7%) as the most common mutations.

Table 1. Sociodemographic and Clinical Characteristics Respondents (n=86)

Variable	n	%
Gender		
Male	32	37.2
Female	54	62.8
Age		
<60 years old	44	51.2
≥60 years old	42	48.8
Staging Cancer		
Stage II	5	5.1
Stage III	1	1.2
Stage IV	64	74.4
Data not available	16	18.6
Immunohistochemistry Result		
ALK positive	11	12.8
EGFR positive (type of mutation not mentioned)	7	8.1
EGFR exon 19	45	52.3
EGFR exon 21 (total)	23	26.7
Unspecified exon 21	18	20.9
L858R mutation	4	4.7
L861Q mutation	1	1.2
Type of EGFR-TKIs or ALK Inhibitors		
Afatinib	21	24.4
Alectinib	6	7.0
Brigatinib	1	1.3
Crizotinib	3	3.5
Erlotinib	17	19.8
Gefitinib	11	12.8
Lorlatinib	1	1.2
Osimertinib	26	30.2
Number of side effects experienced		
None	49	57.0
One side effect	20	23.3
Two side effects	13	15.1
Three side effects	4	4.7
Smoking History		
Smoker	16	18.6
Non-Smoker	47	54.7
Data not available	23	26.7
Education		
Low	5	5.8
Moderate	19	22.1
High	51	59.3
Data not available	11	12.8
Number of Comorbidities		
None	44	51.2
One	19	22.1
Two	13	15.1
Three and more	10	11.6
Polypharmacy		
≥5 items	35	40.7
<5 items	51	59.3
Caregiver Status		
Yes	37	43.0
No	49	57.0

Table 2. Type of Metastases of NSCLC patients (n=101*)

Type of Metastatic	n	%
Bone	34	32.67
Brain	22	21.78
Liver	4	3.96
Lymph Node	3	2.97
Pleura	3	2.97
Spine	6	5.94
Peritoneum	1	0.99
Adrenal	1	0.99
None	27	26.73

Note: *One patient can have more than one type of metastasis

These results align with the sociodemographic data, which show that targeted therapy was dominated by third-generation EGFR-TKIs, namely Osimertinib (30.2%), and by second-generation EGFR-TKIs, namely Afatinib (24.4%). Most NSCLC patients (57.0%) did not report serious events while taking EGFR-TKIs or ALK Inhibitors.

Table 3. Adherence Level with Sociodemographic Data of Respondents (n=86)

Variable	MPR Score		*P*
	Adherence (≥0.8)	Non-Adherence (<0.8)	
Gender			
Male	31 (36.05%)	1 (1.16%)	0.145
Female	46 (53.49%)	8 (9.30%)	
Age			
<60 years old	35 (40.70%)	7 (8.14%)	0.085
≥60 years old	42 (48.84%)	2 (2.33%)	
Staging Cancer			
Stage II	5 (5.81%)	0 (0.00%)	
Stage III	1 (1.16%)	0 (0.00%)	0.853
Stage IV	57 (66.28%)	7 (8.14%)	
Data not available	14 (16.28%)	2 (2.32%)	
Polypharmacy			
≥5 items	29 (33.72%)	6 (6.98%)	0.150
<5 items	48 (55.81%)	3 (3.49%)	
Caregiver Status			
Yes	31 (36.05%)	6 (6.98%)	0.165
No	46 (53.49%)	3 (3.49%)	
Education Level			
None	10 (11.63%)	1 (1.16%)	
Low	3 (3.49%)	2 (2.33%)	0.168
Moderate	17 (19.77%)	2 (2.33%)	
High	47 (54.65%)	4 (4.65%)	
Number of side effects experienced			
None	46 (53.49%)	3 (3.49%)	
One side effect	17 (19.77%)	3 (3.49%)	0.251
Two side effects	10 (11.63%)	3 (3.49%)	
Three side effects	4 (4.65%)	0 (0.00%)	
Number of Comorbidities			
None	41 (47.67%)	3 (3.49%)	
One	15 (17.44%)	4 (4.65%)	0.146
Two	13 (15.11%)	0 (0.00%)	
Three and more	8 (9.30%)	2 (2.32%)	

Table 4. Correlation between Adherence to Targeted Therapy Consumption with Total Treatment Cost (n=86)

MPR Score	n	Median	Min-Max	*P*
Adherence (≥0.8)	77 (89.53%)	Rp.174,811,494.00	Rp.400,000.00 – Rp.2,558,025,557.00	0.955
Non-Adherence (<0.8)	9 (10.47%)	Rp.195,219,088.00	Rp 8,446,365.00 – Rp957,986,621.00	

Table 5. Analysis of Total Treatment Costs for Adherence and Non-adherence Patients in the Use of Targeted Therapy (n=86)

Type of Cost	Adherence (n=77) (Median [Min-Max])	Non-adherence (n=9) (Median [Min-Max])	*P*
Targeted Therapy Costs	Rp 106,040,948.00 (Rp 300,000.00 – Rp 2,404,221,447.00)	Rp 129,314,450.00 (Rp 7,583,794.00 – Rp 892,081,983.00)	0.764
Physician Consultation Costs	Rp 1,960,000.00 (0 – Rp 20,358,000.00)	Rp 2,950,000.00 (0 – Rp 25,520,000.00)	0.994
Supportive Treatment Costs	Rp 1,534,359.00 (0 – Rp 291,033,811.00)	Rp 1,534,359.00 (0 – Rp 93,576,265.00)	0.557
Hospitalization Costs	0 (0 – Rp 42,500,000.00)	0 (0 – Rp 41,122,000.00)	0.909
Laboratory Costs	Rp 450,000.00 (0 – Rp 65,735,000.00)	Rp 11,550,000.00 (0 – Rp 100,181,100.00)	0.704
Radiology Costs	Rp 2,966,400.00 (0 – Rp 74,488,720.00)	Rp 2,966,400.00 (0 – Rp 41,966,500.00)	0.959
Diagnostic Costs	Rp 1,303,000.00 (0 – Rp 74,051,000.00)	Rp 15,624,906.00 (0 – Rp 123,906,500.00)	0.056
Surgical Costs	0 (0 – Rp 66,741,549.00)	0 (0 – Rp 87,948,470.00)	0.769
Total Direct Medical Costs	Rp 164,346,688.00 (Rp 400,000.00 – Rp 2,502,318,800.00)	Rp 192,465,209.00 (Rp 8,446,365.00 – Rp 955,232,742.00)	0.989
Total Indirect Medical Costs	Rp 231,429.00 (0 – Rp 55,302,000.00)	Rp 214,071.00 (0 – Rp 11,700,000.00)	0.745
Total Opportunity Costs	Rp 50,595.00 (0 – Rp 404,757.00)	Rp 67,460.00 (0 – Rp 202,379.00)	0.152

Based on Table 3, the adherence and non-adherence groups had similar profiles of characteristics. There was no statistically significant association between adherence and gender (*P*=0.145), age (*P*=0.085), staging cancer (*P*=0.853), number of comorbidities (*P*=0.146), polypharmacy (*P*=0.150), caregiver presence (*P*=0.165), education received (*P*=0.168), and number of side effects (*P*=0.251).

Table 4 shows that 77 of 86 NSCLC patients (89.53%) demonstrated high adherence, as indicated by an MPR ≥0.8. However, the Mann-Whitney test revealed no significant difference in total treatment cost between patients adhering to targeted therapy and those not adhering (*P*=0.955), despite an approximately IDR 20 million difference.

Table 5 presents a detailed breakdown of total treatment costs, including direct medical costs, indirect medical costs, and opportunity costs for NSCLC patients who were adherent or non-adherent to targeted therapy, which was analyzed using the Mann–Whitney test. The difference in total direct medical costs between adherent and non-adherent patients was approximately ±28.1 million rupiah. However, this difference was not statistically significant (*P*=0.989). Furthermore, no statistically significant differences were observed in indirect medical costs (*P*=0.745) or opportunity costs (*P*=0.152).

DISCUSSION

Table 1 indicates that the highest consumption of targeted therapy drugs occurred among stage four NSCLC patients, specifically those with EGFR exon 19 deletion. This study aligned with research suggesting that EGFR exon 19 deletions and L858R mutations are the most common in the Asian population.[12] According to NCCN guidelines, patients with NSCLC and EGFR mutations are recommended to receive EGFR-TKIs, particularly Osimertinib, particularly for those with EGFR exon 19 or 21 deletions.[13]

Table 1 also show most patients with NSCLC (59.3%) were prescribed fewer than five types of medications. This is likely because most patients (51.2%) had no comorbidities and therefore did not

require a caregiver to manage their targeted therapy or supportive medications (57.0%). Meanwhile, Table 2 shows that metastases occur primarily in the bone and brain in patients with NSCLC. This is in line with NSCLC patients, who mostly experience metastases in the brain (30–50%) and bones (30–40%), and is associated with higher mortality.[14]

According to Table 3, nearly 90% of NSCLC patients demonstrated high compliance with EGFR-TKI and ALK inhibitor therapy, indicated by an MPR value of 0.8 or higher. Other studies support this, indicating that adherence to targeted therapy enhanced treatment efficacy compared to chemotherapy.[15] EGFR-TKIs and ALK Inhibitors are generally administered once daily, except for Alectinib, which is taken twice daily at a dose of 600 mg, and Brigatinib, which is initiated at 90 mg once daily for the first 7 days, followed by a maintenance dose of 180 mg once daily.[13]

Table 3 also shows that differences in characteristics between NSCLC patients with adherence and those with non-adherence can be compared. This study found no correlation between adherence to targeted therapy and gender or age, differing from previous research showing that elderly patients (≥60 years) with swallowing difficulties tend to have low adherence.[16] However, other studies noted that EGFR-TKIs and ALK inhibitors can be administered in liquid form or via feeding tubes, which may support adherence.[17]

The NSCLC patients in any staging who have comorbidities or consumed more than or equal to 5 types of supportive drugs did not affect drug compliance. Some NSCLC patients also remained compliant in consuming drugs even without the help of caregivers. Other studies show that lung cancer elderly patients who experience polypharmacy have a low risk of compliance due to the risk of drug-drug interactions and adverse effects.[18] The presence of family members or caregivers who monitor patients during targeted therapy is vital to compliance.[19]

Some NSCLC patients did not experience side effects while taking targeted therapy. In advanced breast cancer patients undergoing targeted therapy, specifically with agents such as CDK4/6 inhibitors in the context of polypharmacy, reduced patient adherence often occurs due to adverse effects like QT prolongation, highlighting the significant role caregivers play in enhancing compliance.[20,21]

This study found that education level did not significantly affect medication adherence, indicating that patients across all educational backgrounds—from low to high—maintained adherence to targeted therapy. In contrast, another study has revealed that the role of education level influences drug adherence, such as in breast cancer patients who consume Capecitabine, with or without intravenous chemotherapy.[22]

Table 4 indicates that high adherence did not significantly increase total treatment costs, with a difference of approximately IDR. 20 million relative to patients with low adherence. In contrast, non-adherence with targeted therapies such as EGFR-TKIs was associated with increased treatment costs and a higher likelihood of disease progression.[16]

Table 4 also shows that the maximum target therapy cost is up to IDR. 2 billion, as patients continued to take target therapy drugs from January 2023 to March 2025. This finding is worrying, as patients with chronic illnesses in Indonesia—such as kidney disease, liver disorders, asthma, and hypertension—tend to have low adherence rates, reported at around 57%. Sociodemographic factors and treatment costs contribute to this poor adherence.[23] However, patients who did not receive EGFR-TKI or ALK inhibitor therapy at the research site were excluded from the study, as the researchers could not monitor their adherence to targeted therapy.

Table 5 further supports the finding that non-adherent NSCLC patients incurred higher total treatment costs than adherent patients, with a difference of approximately ±28.1 million Indonesian rupiah. The increased expenses observed among non-adherent patients were primarily attributable to disease progression, which necessitated more frequent physician consultations. In several cases, non-adherent NSCLC patients were also advised to undergo repeated laboratory tests and diagnostic evaluations to monitor cancer progression. Notably, the cost of FDG-PET/CT

examinations accounted for a substantial share of diagnostic expenditures among non-adherent respondents, underscoring the need to assess metastatic spread associated with disease progression.

Table 5 also shows that no statistically significant differences were observed in indirect medical costs (P=0.745) or opportunity costs (P=0.152) between adherent and non-adherent groups. These findings suggest that the magnitude of indirect medical costs and opportunity costs incurred due to hospital visits did not represent a barrier to adherence to EGFR-TKI or ALK inhibitor targeted therapy. This remained the case despite additional expenses for transportation, caregiver services, and time lost during physician consultations. In some instances, the increase in total treatment costs among cancer patients receiving oral targeted therapy has been reported to range from USD 106 to USD. 749.[24]

A key strength of this study is that it addresses a previously unexplored area in Indonesia. Another highlight was further research on the relationship between adherence to EGFR-TKI and ALK inhibitor therapy in patients with NSCLC and the associated total treatment costs.

LIMITATION

This study has several limitations that should be considered when interpreting the findings. The reliance on secondary data derived from hospital medical records may have limited the completeness and granularity of clinical and behavioral information, while excluding NSCLC patients who did not obtain their medications from the hospital pharmacy may have constrained the generalizability of the results. Moreover, the analysis did not address the association between therapeutic efficacy and total treatment costs, thereby limiting the ability to evaluate the impact of clinical outcomes on economic burden.

CONCLUSION

Among NSCLC patients receiving EGFR-TKIs or ALK inhibitors, 89.53% demonstrated adherence to their prescribed therapy. Compliance with targeted therapy was not significantly associated with patient characteristics such as gender, age, cancer stage, polypharmacy, caregiver support, educational attainment, or experienced side effects. Accordingly, future qualitative studies are warranted to more thoroughly investigate patient- and system-level determinants of adherence, and prospective studies incorporating standardized measures of adherence, therapeutic efficacy, and clinical outcomes are recommended to enable a more comprehensive and rigorous assessment of treatment compliance and its clinical and economic implications.

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CONFLICT OF INTEREST

The authors affirm that they have no conflict of interest.

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