

**Original Article**

# The survival rate comparison of non small cell lung carcinoma patients who are given by epidermal growth factor receptor-tyrosin kinase inhibitor and those given by first-line chemotherapy treatment

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**ABSTRACT**

**Introduction.** Lung cancer is the type of non-small cell carcinoma (NSCLC) consists of non-squamous and squamous. Non-small cell lung cancer of non squamous types consist of adenocarcinoma and large cell carcinoma. Currently, lung cancer therapy is highly developed of chemotherapeutic agents to targeted therapy especially EGFR-TKI. This study aims to assess the survival rate of NSCLC patients who receive first line chemotherapy and those who receive EGFR-TKI therapy at Wahidin Sudirohusodo hospital. **Methods.** This study is a retrospective study between 2017 to 2019 from the medical records of NSCLC patients who receive first-line chemotherapy and those who receive EGFR-TKI. Patients with platinum-based chemotherapy and EGFR-TKI with gefitinib therapy 1x250 mg/day or erlotinib 1x150mg/day and or afatinib 1x40 mg/day. Survival rate assessed from start to erect the diagnosis until the patient dies or when the study is discontinued. **Result.** From 239 subject of NSCLC patients consisted of 135 patients who receive first-line chemotherapy, and 104 patients are treated with

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*EGFR-TKI. Based on the characteristics of the patients, most are more than 40 years old (chemotherapy 124 (91.9%) and EGFR-TKI 101 (97.1%) with the male gender that dominates (chemotherapy 98 (72.6%), EGFR-TKI 64 (61.5%). Smoking patients who received first-line chemotherapy are 65.2% and 61.5% of EGFR-TKIs with chemotherapy highest IB (severe IB 28.9%) and for EGFR-TKI (moderate IB are 26.9%). 73.2% of adenocarcinoma histology type with a predominance of stage IV 86.6% (83.7% for chemotherapy and EGFR-TKI 90.4%). Survival rate of patients are 98,7% for 6 months survival, 1 year survival rate is 94.1% and 2 years survival rate of 24.3%. Median survival patients who receiving EGFR-TKI longer than they received first- line chemotherapy (21 months versus 20 months). The 18 months PFS showed that patients treated with EGFR-TKI were 15 months, while patients receiving chemotherapy was 11 months. (P 0.000). **Conclusion.** Survival rates in NSCLC patients with EGFR-TKI therapy had significantly the highest survival rates compared with all other chemotherapy. Progression was faster in patients with first-line chemotherapy than EGFR-TKI. The factors that most influence the survival rate is type of therapy with p value<0.05.*

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## 1. INTRODUCTION

Lung cancer is the second most common cancer and the leading cause of cancer death in the United States. It is estimated that there will be 247,270 new cases of lung cancer in 2020, with 130,340 male cases and 116,930 female cases. In Indonesia, in 2020 lung cancer contributed to the mortality percentage of up to 11.4% of total cancer deaths, and it is predicted that new cases will increase by 83% from 2018 to 54,983 in 2040.<sup>1</sup>

Lung Cancer type Non-Small Cell Carcinoma (NSCLC) represents approximately 80% of the total pulmonary malignancies and most of these patients with NSCLC are in an advanced stage and have a poor prognosis.<sup>2</sup> The poor prognosis of lung cancer is caused by many factors, especially the advanced stage of the disease when the diagnosis can be made, data from the Wahidin Sudirohusodo Hospital shows that patients who have been diagnosed with lung cancer are on stages IIIB and IV.

During the last 20 years, a number of efforts have been made to reduce mortality in lung cancer patients, such as the use of surgical therapy, radiotherapy, combination chemotherapy or a combination of all. However, the improvement in survival is still small.<sup>2,3,4</sup> Conventional chemotherapeutic agents work by non-specifically inhibiting cancer cells, causing toxicity not only to cancer cells but to normal cells. The therapeutic paradigm has shifted to become more rational towards targeted therapy. Targeted

therapy attacks cancer cell elements that are important for the growth or survival of cancer cells, and prevents severe side effects due to conventional cytotoxic administration. Targeted therapeutic agents that act to block the epidermal growth factor receptor and signaling pathway tyrosin kinase inhibitors (EGFR-TKI) such as gefitinib, erlotinib and afatinib, have been introduced and serve as examples of a therapeutic paradigm shift.<sup>5</sup>

Clinical application of EGFR-TKI therapy has been carried out and has been reported to increase survival rates of more than 30 months in patients with advanced NSCLC lung cancer.<sup>6</sup> On the other hand, Tomasini.P et al showed that survival and PFS were longer with chemotherapy compared to EGFR-TKI. Therefore, information is needed regarding the efficacy of EGFR-TKI therapy and chemotherapy along with the development of a wide variety of therapeutic agents used.<sup>7</sup> This study attempts to compare the survival of NSCLC patients who received EGFR-TKI and those who received first-line chemotherapy at the Wahidin Sudirohusodo Hospital (RSWS) Makassar

## **2. METHODS**

This retrospective cohort study was conducted at the Wahidin Sudirohusodo Hospital (RSWS) Makassar, by collecting medical records and electronic health records of all NSCLC patients receiving EGFR-TKI therapy (gefitinib and erlotinib, afatinib) or first-line chemotherapy (carboplatin and paclitaxel, carboplatin and etoposide, carboplatin and vinorelbine). Samples were collected consecutively through a list of patients who received first-line chemotherapy and EGFR-TKI targeted therapy from January 2017 to December 2019. Inclusion criteria were all patients diagnosed with NSCLC who received EGFR-TKI targeted therapy or first-line chemotherapy since January 2017- December 2019 and willing to participate in the research. Exclusion criteria were patients diagnosed with squamous cell carcinoma, and patients diagnosed with stage I-IIIa NSCLC who had undergone surgery and were analyzed. This research has been approved by the Research Ethics Committee of the Faculty of Medicine, Unhas and has received permission from RSWS. Follow-up was carried out for 2 years.

Histologic subtypes of lung cancer were determined by assessing lung tissue obtained by Trans-Thoracic Needle Aspiration (TTNA), Trans-Bronchial Lung Biopsy (TBLB), bronchial lavage, bronchial swab, bronchial biopsy, fine needle biopsy, pleural fluid cytology and pleural biopsy. confirmed by histopathological examination. Lung cancer staging was made according to the TNM 8 classification.

During the first visit, age, sex, ethnicity, smoking history, comorbidities, and stage were recorded. Clinical examination, laboratory examination, abdominal ultrasonography, and computed tomography scan were also performed at the first visit, after three cycles of chemotherapy and at the end of six cycles of chemotherapy to determine treatment response. The same was done in patients receiving targeted EGFR-TKI therapy. Treatment response was assessed based on the Response Evaluation Criteria in Solid Tumor (RECIST V1.1) criteria. Survival at 6 months, 1 year and 2 years was evaluated after the first chemotherapy session.

Total sampling was used in recruiting the subjects of this study, as many as 290 samples. Chi-square or Fisher's exact test was performed to compare sex, age, ethnicity, smoking history, Brinkman index, staging, and histological type by type of therapy. The

chi-square test or Fisher's exact test was performed to identify prognostic factors associated with 2-year survival and treatment response. Relative risk (RR) and 95% confidence interval (CI) were also calculated. All analyzes were performed on SPSS, version 24.0 (IBM Corp, USA). Then the survival analysis was carried out using the Kaplan-Meier product limit. The log-rank test was used to obtain the difference between the sub-variables. Significance was determined by the value of  $p < 0.05$ .

### 3. RESULTS

The total number of Non-Small Cell Lung Carcinoma (NSCLC) patients recorded from 2017-2019 at Wahidin Sudirohusodo Hospital was 290. The number of patients who did not meet the study criteria was 51 people so that the total subjects in this study were 239 people, consisting of 135 people who received first-line chemotherapy and 104 people who received EGFR-TKI therapy. Chemotherapy is given in 3-week or 21-day cycles while EGFR-TKI therapy (gefitinib, erlotinib, afatinib) is given daily. In this study, survival was assessed from the time the patient was diagnosed with NSCLC until the patient died or the study was completed.

Table 1 shows the characteristics of patients who received first-line chemotherapy consisting of 98 men (72.6%) and 37 women (27.4%) while EGFR-TKI therapy consisted of 64 men each (61.5%) and 40 women (38.5%). Based on age, 124 people (91.9%) received first-line chemotherapy and 101 people received EGFR-TKI (97.1%). Patients who received first-line chemotherapy smoked 88 people (65.2%) and who received EGFR-TKI 64 people (61.5%) with Brinkmann Index (IB) patients who received first-line chemotherapy were 22 mild IB (16, 3%), moderate 27 people (20%) and severe 39 people (28.9%), while the IB of patients receiving EGFR-TKI therapy was mild 12 people (11.5%), moderate 28 people (26.9%) and the weight of 24 people (38.5%). In this study, the most ethnic groups who received chemotherapy lines I and EGFR-TKI were Bugis. Based on the stage, patients who received chemotherapy and EGFR-TKI mostly stage IV 113 people (83.7%) and 94 people (90.4%). Based on the type of histology, it was found that patients who received first-line chemotherapy were adenocarcinoma 100 people (74.1%) and non-small cell carcinoma 35 people (25.9%) while patients treated with EGFR-TKI were adenocarcinoma 75 people (72.1%) and Non-Small Cell Carcinoma 29 people (27.9%).

#### Survival analysis (Kaplan-Meier)

Based on time from diagnosis of lung cancer to the death of the patient or the end of the study, the results of the survival of the NSCLC patient were obtained using the method of survival analysis Kaplan-Meier. In this study, 58 patients (24.3%) lived until the end of the study, with details of 30 (51.7%) being NSCLC patients receiving chemotherapy and 28 (48.3%) receiving EGFR-TKI therapy.

Table 2 shows the median survival and 2-year survival based on the characteristics of patients with NSCLC who received first-line chemotherapy and EGFR-TKI. In this study, almost all variables based on age, gender, smoking history, and staging had a median survival of 19-20 months. Meanwhile, based on therapy, the first-line chemotherapy was median survival of between 19-20 months, except for the carboplatin and etoposide regimens, which was only 15 months. EGFR-TKI From the table we can see that the median survival for erlotinib is 23 months, afatinib is 22 months

and gefitinib is 20 months.

**Table 1. Characteristics of the sample**

Characteristics	first-line chemotherapy, N (%)	EGFR-TKI, N (%)	N (total)	%
<b>Gender</b>	<b>n=135</b>	<b>n=104</b>	<b>n=239</b>	
Male	98 (72,6)	64 (61,5)	162	67,8
Female	37 (27,4)	40 (38,5)	77	32,2
<b>Ethnic</b>				
Bugis	49 (53,8)	42 (46,2)	91	38,1
Makassar	45 (60,8)	29 (39,2)	74	31,0
Toraja	15 (60,0)	10 (40,0)	25	10,5
Mandar	2 (50,0)	2 (50,0)	4	1,6
Lain-lain	24 (53,3)	21 (46,7)	45	18,8
<b>Age</b>				
< 40 Years	11 (8,10)	3 (2,90)	14	5,9
≥ 40 years	124 (91,9)	101 (97,1)	225	94,1
<b>Smoke history</b>				
ya	88 (65,2)	64 (61,5)	152	63,6
tidak	47 (34,8)	40 (38,5)	87	36,4
<b>Indeks Brinkman</b>				
mild	22 (16,3)	12 (11,5)	34	22,4
moderate	27 (20,0)	28 (26,9)	55	36,2
severe	39 (28,9)	24 (23,1)	63	41,4
<b>Stages</b>				
< IV	22 (16,3)	10 (9,60)	32	13,4
≥ IV	113 (83,7)	94 (90,4)	203	86,6
<b>Histology type</b>				
Adenokarsinoma	100 (74,1)	75 (72,1)	175	73,2
Karsinoma BSK	35 (25,9)	29 (27,9)	64	26,8

**Table 2. Survival based on characteristics of NSCLC patients at Wahidin Sudirohusodo Hospital Makassar**

Variable	median survival (month)	95% CI		2 years Survival		P value	
		Min	Max	Died, N%	survive, N%		
Gender	Male	20	19,4	20,7	125 (77,2)	37 (22,8)	0,539
	Female	20	18,7	21,4	56 (72,7)	21 (27,3)	
Age	≤ 40 tahun	21	19,4	22,6	13 (76,5)	4 (23,5)	0,653
	> 40 tahun	20	19,4	20,6	168 (75,7)	54 (24,3)	
Ethnic	Bugis	20	19,0	20,9	71 (78,0)	20 (22,0)	0,958
	Makassar	20	19,1	20,9	53 (71,6)	21(28,4)	
	Toraja	19	18,0	20,0	21 (84,0)	4 (16,0)	
	Mandar	15	9,8	20,2	4 (100)	0 (0,0)	
	Others	20	19,4	20,6	32 (71,1)	13 (28,9)	
Smoke	Yes	20	19,3	20,7	120(78,9)	32 (21,1)	0,078
	No	21	19,6	22,4	61 (70,1)	26 (29,9)	
IB	Mild	21	18,2	23,8	21 (63,6)	12 (36,4)	0,058
	Moderate	20	18,8	21,1	45 (81,8)	10 (18,2)	
	Severe	19	17,9	20,0	50 (83,3)	10 (16,7)	
Staging	< IV	19	17,9	12,1	26 (81,3)	6 (18,8)	0,348
	≥ IV	20	19,3	20,7	155(74,9)	52 (25,1)	
Therapy							
Chemo I	Carbo+vinorelbine	19	17,9	20,0	64 (79,0)	17 (21,0)	0,043
	Carbo+paklitaxsel	20	19,1	20,8	35 (75,5)	12 (25,5)	
	Carbo + etoposide	15	13,7	16,2	6 (85,7)	1 (14,3)	
EGFR-TKI	Gefitinib	20	18,7	21,3	59 (75,6)	19 (24,4)	0,043
	Erlotinib	23	22,1	23,8	13 (65,0)	7 (35,0)	
	Afatinib	22	19,6	24,0	4 (66,7)	2 (33,3)	

### Progression-Free Survival (PFS)

In Figure 1 shows Progression-Free survival (PFS) at 12 months of observation in patients given EGFR-TKI therapy showed that there was no disease progression of more than 50%, whereas in patients receiving chemotherapy it showed more than 50% of patients progressed at month 11.

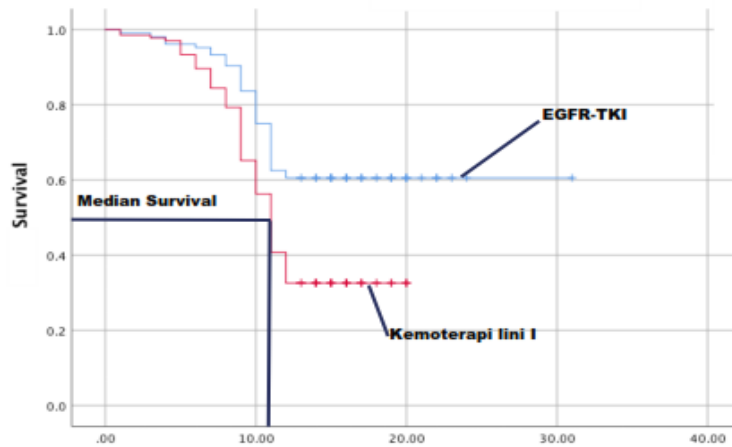


Figure 1. Progression-Free survival 12-month.

The observation progression-Free Survival 18 month (figure 2) showed that the median survival of patients treated with EGFR-TKI was 15 months, while patients receiving chemotherapy was 11 months. Based on log rank analysis, it was found that there was a significant difference in 18-month PFS with a p value of 0.000 for EGFR-TKI therapy and chemotherapy.

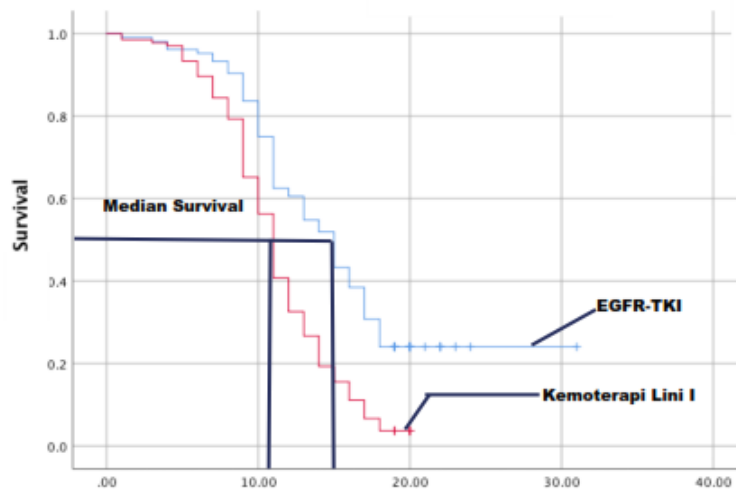


Figure 2. Progression-free survival for 18 months

### 2-years Survival

overall survival of non-squamous NSCLC patients receiving first-line chemotherapy and EGFR-TKI therapy as shown in Figure 3 shows that the survival of patients receiving EGFR-TKI therapy was significantly different compared to that of patients receiving chemotherapy (P value 0.043). The median survival of patients given EGFR-TKI was longer (21 months) than the median survival of patients receiving chemotherapy (20 months). Based on the comparison of chemotherapy, non-squamous NSCLC patients who received EGFR-TKI had a median survival of 21 months with a 2-



year survival rate of 26.9%, while those receiving first-line chemotherapy had a median survival of 20 months with a 2-year survival rate of 22.2%.

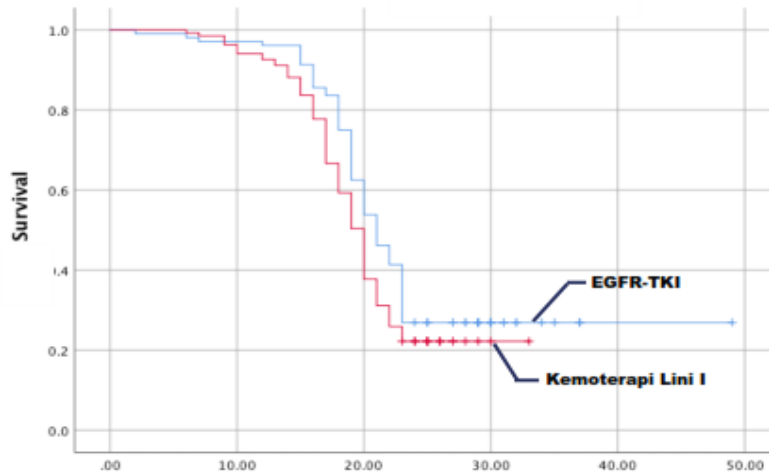


Figure 3. The survival of NSCLC patients who received first line chemotherapy and who received EGFR-TKI line I at Wahidin Sudirohusodo Hospital Makassar.

### Bivariate Analysis

In this study, researchers conducted a bivariate analysis to see the relationship and magnitude of the relationship between the survival of non-squamous NSCLC patients who received first-line chemotherapy and those who received EGFR-TKI therapy and the factors considered to be influencing using regression analysis Cox. In table 3, we can see that the factor that is considered the most influential on the survival of NSCLC patients receiving first-line chemotherapy and EGFR-TKI therapy is the Briknman index with a p value <0.22, especially the type of therapy with a hazard ratio (HR) of 2.05. ; 95%CI 1.01-4.12 ; p<0.046 and therapy (HR 1.15; 95%CI 0.92-1.45, p-value <0.22).

Table 3. Bivariate analysis with Coxregression

Bivariate variables	HR	95% CI	P
Gender	1,11	0,77-1,57	0,60
Age	1,37	0,76-2,49	0,30
Ethnic	0,97	0,86-1,10	0,66
Smoke	1,09	0,60-1,90	0,77
Index Brinkman	1,15	0,92-1,45	0,22
Stage	0,88	0,58-1,35	0,57
Types of therapy	2,05	1,01-4,12	0,046
Monoteraphy	1,15	0,92-1,45	0,22



#### 4. DISCUSSIONS

In this study, data obtained from 239 lung cancer patients with non-small cell carcinoma (NSCLC) which were divided into 135 patients who received first-line chemotherapy and 104 patients who received EGFR-TKI. The mean age of the patients in this study was 57.82 years with the youngest being 28 years old and the oldest being 91 years old. In this study, it was found that most of the NSCLC who received first-line chemotherapy and were treated with EGFR-TKI were more than 40 years old and the male sex was more dominant. Lung cancer is known as a gene disease that often occurs at the age above 40. This is in accordance with the research of Goss G et al.<sup>8</sup> or Kim ES et al.<sup>9</sup> and also Sandler A et al.<sup>10</sup> Age at diagnosis affects the prognosis of lung cancer. Increasing age causes the accumulation of carcinogenic substances in the body and genetic damage. In addition, increasing age causes a decrease in immunity, decreases DNA repair and causes a loss of cell regulation that facilitates carcinogenesis in the body. Each 10-year increment increases the risk of death by 30%.<sup>3,11</sup>

male gender still dominates NSCLC patients according to risk factors for lung cancer are men with the age of more than 40 years. These results are in line with the research of Elisna, et al.<sup>12</sup> which got the number of men by 71.4% and the study of Lee, et al.<sup>13</sup> of 77.5%. Factors such as genetic susceptibility related to sex or sex hormones are thought to be associated with a higher incidence of lung cancer.<sup>1</sup> In this study, the ethnic group that suffered the most from NSCLC who received first-line chemotherapy and was treated with EGFR-TKI was the Bugis. Researchers did not find literature discussing the relationship between ethnicity and the incidence of lung cancer, especially in Indonesia, so it was deemed necessary to explore the relationship between ethnicity and the incidence of lung cancer, especially NSCLC.

In this study 65.2% of patients with NSCLC who received first-line chemotherapy and 61.5% of patients who received EGFR-TKI were smokers. Most smoking patients are male. The subjects of this study who smoked had a dominant severe IB, namely 28.9% of patients receiving chemotherapy and moderate IB, which was 26.9% who were treated with EGFR-TKI. Unfortunately, our study was not equipped with the types of cigarettes used by the subjects. This is in accordance with the risk factors for lung cancer which are directly related to smoking duration, number of cigarettes, degree of inhalation, tar and nicotine content, and use of unfiltered cigarettes. However, this incident can also occur in passive smokers, especially in young women.<sup>11,14</sup>

Based on cell type, the predominance of adenocarcinoma in this study is in accordance with the research of Inoue et al.<sup>15</sup> and Mok TS et al.<sup>8</sup> and data from Wahidin Sudirohusodo Hospital in this study between 2017 and 2019 were 73.2% (74.1% treated with first-line chemotherapy and 72.1% treated with EGFR-TKI). This data is also higher with the data at the persahabatan Hospital in 2004-2006, lung cancer patients with adenocarcinoma type still dominate at 56.3%. Unlike the White et al studies<sup>17</sup> that non-squamous NSCLC more dominant large cell carcinoma (28%) compared to adenocarcinoma (22%).<sup>7,8</sup>

Nearly 70% of lung cancer patients present with local symptoms due to the tumor and the presence of metastases. This is because the initial picture of the clinical course is usually asymptomatic. If the patient has shown symptoms, then the patient is at a more advanced stage.<sup>16</sup> This is in accordance with the demographic picture in this study which found that patients who were at stage IV were 83.7% and the average metastases to the

pleura. Likewise, the distribution stage of the patient's disease in this study was in accordance with the research of Rossel et al.<sup>17</sup> who received advanced stage (IV) nonsquamous NSCLC 86.6% more than stage III 13.4%. Research Crino et al.<sup>18</sup> also get 80% stage IV dominance compared to stage IIIB 20%. Research conducted by the Southwest Oncology Group (SWOG)<sup>19</sup> only found 11-12 % of patients with stage III NSCLC, the rest were stage IV (88-89%) which is in accordance with the theory that around 70% of patients with NSCLC, especially nonsquamous, are in an advanced stage (metastasis).

Based on the type of therapy, NSCLC patients in this study received the most type of first-line chemotherapy, which was carboplatin+vinorelbine (33.9%) followed by carboplatin+paclitaxel 19.7% and carboplatin+etoposide 2.9%. The types of chemotherapy used in this study were all in accordance with the administration of chemotherapy based on platinum-based therapy. The minimum administration of chemotherapy is 2 cycles and a maximum of 6 cycles.<sup>2,20</sup> While the administration of EGFR-TKI in this study was dominated by gefitinib in 78 patients. This is because the use of erlotinib is still very rare. The administration of EGFR-TKI in this study paid attention to or saw whether the patient had previous mutations, this was based on the NCCN guidelines that all NSCLC patients who will be given EGFR-TKI therapy must be checked for mutations.<sup>21</sup> The Indonesian Lung Doctors Association (PDPI) itself recommends the use of first-line EGFR-TKI based on the 2005 Bukit Tinggi consensus that EGFR-TKI can be given as definitive (first-line) treatment if the patient for various reasons cannot or refuses chemotherapy.<sup>20</sup>

Kaplan Meir's analysis in this study showed that there was a significant difference in 2-year survival between the EGFR-TKI group and the first-line chemotherapy group, which were 20 and 21 months, respectively ( $p < 0.043$ ). As was the case with this study, Fiala. O et al.<sup>22</sup> studied 54 patients of whom 23 were treated with EGFR-TKI and 31 patients with various first-line chemotherapy regimens. The median survival or median survival was 14.5 months vs. 21.4 months ( $p=0.729$ ). The median PFS in patients treated with EGFR-TKI was 7.2 months vs. 2.5 months in patients treated with chemotherapy ( $p<0.001$ ). Tomasini. P et al found contradicting our results. Tomasini.P et al showed that survival and PFS were longer with chemotherapy compared to EGFR-TKI. Survival was 8.38 versus 4.99 months, respectively (hazard ratio 0.70, 95% CI 0.59 to 0.83;  $p<0.0001$ ) and PFS was 4.30 versus 2, respectively. .83 months (hazard ratio 0.66, 95% CI 0.57 to 0.77;  $p < 0.0001$ ).<sup>7</sup>

6-month and 12-month survival in both patients receiving EGFR-TKI and first-line chemotherapy was still more than 50%. This study is much different from Cancer Research UK in 2010-2011 which got a lung cancer survival rate in the first 1 year of 32.1%.<sup>7</sup> The surveillance, epidemiology and end results (SEER) program in America reported 1 year survival for lung cancer NSCLC stage IV was 15.9%. A study by Ou SH, Ziogas A et al conducted in America on four ethnicities showed that the survival for NSCLC in Asian ethnicities was better than that of non-Asians (HR 0.861, 95% CI: 0.808-0.918,  $p < 0.0001$ ).<sup>24</sup> Even Asian ethnicity remained a favorable prognostic factor for survival among never-smokers (versus non-Asian HR 0.841, 95% CI: 0.728-0.971,  $p < 0.0180$ ) and among smokers (compared non-Asian; HR 0.867, 95% CI: 0.807-0.931,  $p < 0.0001$ ).<sup>23</sup>

Progression-free survival (PFS) at 12 months of observation in patients treated with EGFR-TKI showed that there was no disease progression of more than 50 percent, whereas in patients receiving chemotherapy, more than 50% of patients experienced progression at 11 months. we are almost the same as the study of Kim et al.<sup>9</sup> that there is a superior comparison between EGFR-TKI and chemotherapy, platinum-based which is 7.6 months versus 8 months.

Observation of PFS at 18 months showed that the median survival of patients treated with EGFR-TKI was much better (15 months) than chemotherapy (11 months). From the log rank analysis, it was found that there was a significant difference in 18-month PFS (p value 0.000) in the target therapy compared to chemotherapy. This is in accordance with the research of Chee KL, et al.<sup>26</sup> that EGFR-TKI statistically significantly extended overall Progression-Free survival (PFS) (HR = 0.37, 95% CI = 0.32 to 0.42, P < 0.001) in all subgroups although there was no difference in survival. Overall, between EGFR-TKI and chemotherapy (HR = 1.01, 95% CI = 0.88-1.17, P = 0.84).

The obstacle faced in this study that the researchers could not avoid was that the research design was a retrospective method of medical records of lung cancer patients between 2017 and 2019 so that the data depended heavily on the completeness of medical records. Some medical records are not found complete data. In addition, because this study wanted to determine the survival of patients who received first-line chemotherapy and first-line EGFR-TKI therapy, the researchers had difficulty finding samples, especially EGFR samples TKI (gefitinib, erlotinib, and afatinib). Important data that could be a strong factor influencing survival such as the appearance of patient status (PS), and the type of metastases were very minimally found in the patient's medical record data, so that further analysis could not be done

## 5. CONCLUSION

Survival rates in NSCLC patients with EGFR-TKI therapy had significantly the highest survival rates compared with all other chemotherapy. Progression was faster in patients with first-line chemotherapy than EGFR-TKI. The factors that most influence the survival rate is type of therapy with p value<0.05.

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**Conflict of Interest Statement:**

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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