The one year survival rate of lung adenocarcinoma patients treated with chemotherapy therapy or targeted

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The one year survival rate of lung adenocarcinoma patients treated with chemotherapy or targeted therapy☆

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Abstract

Background: Adenocarcinoma is the most common of lung Cancer. The treatment for early stage of lung Adenocarcinoma (I, II) is surgery. Targeted therapy is given to lung Adenocarcinoma patients with *EGFR-TKI* mutations. Chemotherapy is given to lung Adenocarcinoma patients without *EGFR-TKI* mutations.

Objective: To compare one-year survival of lung Adenocarcinoma patients treated with chemotherapy or targeted therapy.

Methods: This was a prospective study. The subjects were 100 patients with lung Adenocarcinoma.

Results: 1-year Survival of lung Adenocarcinoma patient for one year was 18%. 1-year survival in patients with targeted therapy was higher than chemotherapy, which was 24% vs 9% ($p < 0.01$). 1-Year survival in chemotherapy patients with Carboplatin combined with Vinorelbin was higher than in other chemotherapy drugs ($p > 0.05$). 1-Year survival in patients with *Erlotinib* drug was 45% highest survival rate compared to chemotherapy drugs and other targeted therapy ($p < 0.05$). Patients receiving *Erlotinib* (45%) has the highest survival compared to all types of therapy.

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Conclusion: Lung *Adenocarcinoma* patients receiving *Erlotinib* significantly had the highest survival rate compared to all other targeted therapy drugs and all types of *chemotherapy* drugs.

Introduction

Lung cancer in the United States, approximately 221,130 new cases of lung cancer.[1] In China the incidence of lung cancer is increasing rapidly because China consumes 30% of the world's cigarettes.[2] In Indonesia lung cancer is ranked 4th in cancer.[2] Lung Adenocarcinoma is the most commonly found type of lung Carcinoma.[2] Lung adenocarcinoma therapy depends on the stage of the disease and the general condition of the patient.[3] Surgery is a therapeutic option for early stage *NSCLC* (I, II).[3] The use of chemotherapy in stage IIIa, IV or target therapy is given at stage IV for the treatment of patients with Adenocarcinoma.[3] Lung cancer treatment can be with chemotherapy or targeted therapy.[3] Targeted therapy is given to patients with gene mutations in exon 19 and 21, whereas exon 20 mutations are not recommended.[3]

Chemotherapy is given to patients with pulmonary Adenocarcinoma without an *EGFR* mutation.[3] The definition of target therapy is a type of cancer drug with a selective work target used for lung cancer with *NSCLC*.[3] The advantage of this drug is that it is given more simply, orally (the *EGFR TKI* group).[3] The type that began to be used is a drug that works as an *inhibitor of the epidermal growth factor receptor (EGFR TKI*), among others *Erlotinib, Gefitinib, Afatinib* and other types that are still under research.[3] The *Italian Lung Cancer Multicenter study in the Elderly Study (MILES*) concluded the survival of pulmonary Adenocarcinoma undergoing platinum-based chemotherapy was 6 months to 12 months while the survival using the target therapy was 9–13 months.[4] The survival of lung Adenocarcinoma using the targeted therapy according to Nishie et al. was 15 months.[5] According to Amarasena's study reported that survival was 12 months to 24 months with a platinum-based regimen in lung Adenocarcinoma patients undergoing chemotherapy.[6] According to Bunn et al. the survival of metastatic cancer patients varied from 6 months to 1 year.[3] According to research Kogure et al. survival lung Adenocarcinoma using targets of therapy was 10 months and total survival is 24 months.[7]

We conducted this study to determine the comparison of clinical response and survival in patients with lung Adenocarcinoma who received chemotherapy or targeted therapy.

Method

The research design used was observational analytic research with a prospective design. The study was conducted at Dr. Wahidin Sudirohusodo and network hospital in Makassar. The study was conducted in November 2017 to December 2019. This study was approved by the Ethics Committee of the Faculty of Medicine with reference number: 1118/H4.8.4.5.31/PP36-KOMETIK/2018.

Population

The population in this study were all lung Adenocacinoma patients who received chemotherapy and targeted therapy and undergoing inpatient and outpatient of the hospitals. Inclusion criteria were age between 18 and 60 years, men and women, getting chemotherapy or targeted therapy, is willing to join the study.

Sample collection methods

Sampling was done by consecutive sampling, where patients who met the inclusion criteria were included in this study until the number of samples was met. All patients with lung Adenocarcinoma do a physical examination, chest X-ray, CBC, blood chemistry, and CT Scan Thorax on before chemotherapy and after chemotherapy cycle 3. Lung Adenocarcinoma sa when the cytology results and TTNA or rinsing/bronchial brushings shows the results of Adenocarcinoma. Patients were grouped into two categories based on the examination of *EGFR* in which patients with the *EGFR* mutation and patients without *EGFR* mutation. During treatment patients were followed for the development of treatment. The response of patients assessed from changes in the size of lung cancer after chemotherapy cycles to 3. Based on the survival rate of patients who had received chemotherapy and targeted therapy, patients are grouped into 2 categories namely life and death which are counted in months.

Statistical analysis

The data obtained were analyzed through a computer by using the program *Statistical Package for Social Science (SPSS*) version 22. The statistical analysis conducted was descriptive statistical calculations, frequency distribution and Life Table statistical tests to assess the survival of lung cancer in general and Kaplan–Meier to assess survival lung cancer according to therapy, the test results are significant if $p < 0.05$.

Results

During the 2 years of the study, 100 subjects were found to meet the inclusion criteria. Table 1 shows that lung Adenocarcinoma patients who received targeted therapy were 50 subjects and who received chemotherapy as 50 subjects, aged between 28 and 80 years. Based on the *EGFR* examination, it was found that lung Adenocarcinoma patients who experienced positive mutations in exon 18 were 2 people,

Table 1 Distribution of sample characteristics ($n = 100$).

Variable	n	%
Gender		
Male	64	64.0
Female	36	36.0
Age		
<60 years	68	68.0
≥60 years	32	32.0
Therapy		
Targeted therapy	50	50.0
Chemotherapy	50	50.0
Status		
Death	42	42.0
Life	58	58.0

Table 2 One-year survival table.

Duration of follow-up (months)	Death	Survival (%)
0	0	100
1	3	94
2	2	85
3	2	77
4	1	72
5	0	69
6	5	67
7	2	63
8	3	60
9	2	56
10	2	51
11	4	51
12	16	18

exon 19 was 19 people, exon 20 was 3 people, exon 21 was 10 people, mutation (*Wild Type*) was 13 people.

Table 22 shows, that the 1 year survival of lung Adenocarcinoma patient for one year was 18%.

Table 3 shows the 1-year survival in patients with significantly higher targeted therapy than in chemotherapy, which is 24% compared to 9% with a p value < 0.01.

As seen in Fig. 1 shows at age < 60 years, 1-year survival was found in patients who receive targeted therapy significantly higher than in patients who received chemotherapy, 23% versus 11% (p;< 0.05).

As can be seen in Fig. 2 showing at age > 60 years, it was found that 1 year survival in the targeted therapy was

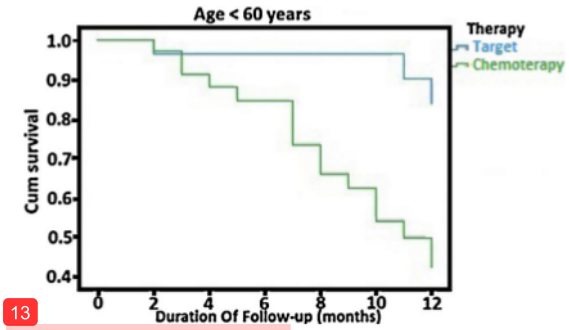

Figure 1 One-year survival by therapy at <60 years of age.

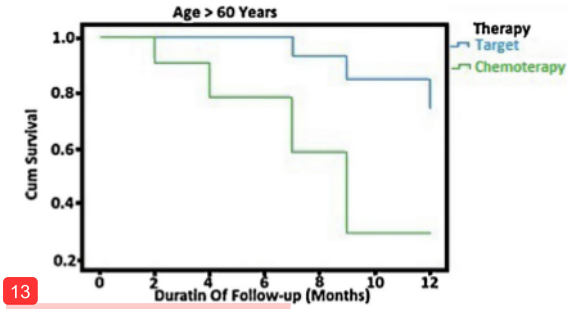

Figure 2 One-year survival by therapy at >60 years of age.

significantly higher than in chemotherapy, which was 26% compared to 0% ($p < 0.05$).

Survival by drug type in chemotherapy

As shown in Table 4, the survival rate of 1 year in patients with Carboplatin combined with Vinorelbin was higher than in other chemotherapy drugs, with p values > 0.05.

Survival by drug type in all samples

As can be seen in Table 5 shows a 1-year survival in patients with *Erlotinib* drug at 45% significantly higher than the survival in other types of target drug therapy or chemotherapy ($p < 0.05$).

Discussion

In this study the survival rate of lung Adenocarcinoma patients were divided into 2 groups. Group of subjects who

Table 3 Survival by therapy.

Therapy	N	Death	Survival estimates			p
			Mean[a]	Median[a]	%	
Targeted therapy	50	19 (38%)	113	12.0	24	0.003
Chemotherapy	50	23 (46%)	8.8	10.0	9	

[a] In months.

Table 4 Survival by drug type in chemotherapy.

Drug type	*N*	Death	Survival estimates			*p*
			Mean[a]	Median[a]	%	
Carboplatin + permetexed	7	4 (57%)	7.6	7.0	0	
Carboplatin + paclitaxel/etoposide	5	2 (40%)	12.8	11.0	0	0.566
Carboplatin + vinorelbin	38	17 (45%)	12.6	11.0	11	

[a] In months.

Table 5 Survival by drug type in all samples.

Types of drugs	*n*	Death	Survival estimates			*p*
			Mean[a]	Median[a]	%	
Afatinib	9	4 (44%)	10.8	12.0	27	
Gefitinib	29	9 (31%)	11.6	12.0	18	
Erlotinib	12	6 (50%)	11.0	12.0	45	0.046
Carboplatin + permetexed	7	4 (57%)	7.2	7.0	0	
Carboplatin + paclitaxel/etoposide	5	2 (40%)	10.4	11.0	0	
Carboplatin + vinorelbin	38	17 (45%)	8.9	11.0	11	

[a] In months.

received chemotherapy and targeted therapies. All subjects were patients with *NSCLC* that resulted from bronkoscopy, Pleural fluid analysis, *Trans Thoracal Needle Aspiration* showing lung Adenocarcinoma. The majority of lung Adenocarcinoma patients who come for treatment after a severe illness or have reached advanced stadium, this shows that there is a suspicion that the process of lung Adenocarcinoma disease has been going on for a long time. Based on the positivity of *EGFR* examination, subjects were divided into 2 groups, namely groups of subjects with positive mutations, and patients without mutations (*Wild Type*). In this study, it was found that there was a 1 year survival rate for lung Adenocarcinoma patients for one year was 18%. The 1-year survival value in this study was also found in patients with significantly higher targeted therapy than chemotherapy, which is 24% compared to 9% with a p value < 0.01.

In this study, 1 year survival was found in male lung Adenocarcinoma patients who received significantly higher therapeutic targets compared to chemotherapy, which was 25% compared to 8% ($p < 0.05$), whereas in lung Adenocarcinoma patients with female, there was no significant difference in 1-year survival between the therapeutic and chemotherapy targets ($p > 0.05$). The result s of this study are supported by research conducted by Han Liang et al. who analyzed data from about 3200 patients in the Cancer Genome Atlas, there are *differences* in molecular characteristics associated with differences in male and female sex in developing tumor therapy and the risk of death rates.[8] From some literature found that Lung Adenocarcinoma patients are more common in male sex than female.[4]

Research at Cipto Mangunkusumo Hospital (RSCM) found that the majority of the younger age had a greater life expectancy.[4] According to Suryanto's research, it was found that lung cancer patients who survived the most were found in the age group of less than or equal to 60 years.[9] However, in this study it was found that 1 year survival at age < 60 years, in patients who received significantly higher therapeutic targets than in patients who received chemotherapy, which was 23% compared to 11% ($p < 0.05$). Whereas at the age of > 60 years, 1 year survival rate was found to be significantly higher in the targeted therapy than in chemotherapy, which was 26% compared to 0% ($p < 0.05$).

In this study a 1 year survival rate in chemotherapy patients with Carboplatin combined with Vinorelbin was higher than in other chemotherapy drugs, but it was not statistically significant with a p value > 0.05. This is consistent with research conducted by the *Southern Italy Cooperative Oncology Group (SICOG)* that the survival rate of patients receiving Gemsitabin (Permetexed) and Vinorelbin combination chemotherapy 29 weeks, whereas in the single group only 18 weeks.[4]

In this study, a 1-year survival rate for patients with *Erlotinib* was 45% significantly higher than the survival in all other types of targeted therapy and chemotherapy drugs ($p < 0.05$). The results of this study are supported by research conducted by this in accordance with the *European Tarceva* vs *Chemotheraphy (EURTAC)* study, which is in a stage 3 multicenter test of 173 patients with active mutation *EGFR* randomly receiving *Erlotinib*, then *Erlotinib* therapy is associated with improvement in the PFS median of 9 months.[9] *Erlotinib* therapy was associated with improved survival of 9 months compared to chemotherapy 5 months.[9,10]

This is in accordance with the *Italian Lung Cancer Multicenter study in the Elderly Study (MILES)* concluded that the survival of pulmonary Adenocarcinoma undergoing platinum-based chemotherapy is 6 months to 12 months while survival using the targeted therapy is 9–13 months.[5]

Conclusion

Survival in lung Adenocarcinoma patients receiving *Erlotinib* targeted therapy (45%) significantly had the highest survival rate compared to all other targeted therapy drugs and all types of chemotherapy drugs.

Conflict of interest

The authors declare no conflict of interest.

References

1. American Cancer Society. Global Cancer Facts & Figures. 3rd Edition. www.cancer.org/cancer/lungcancer [20.10.16].
2. Amin Z, Kanker Paru. Ilmu Penyakit Dalam. 6th Edition. Interna Publishing. Pusat Penerbitan Ilmu Penyakit Dalam. 2014.
3. A Yusuf AW. Pedoman Nasional Untuk Diagnosis Dan Kanker Paru Di Indonesia 2015. 2016.
4. Fawziah A, Sari N. Kesintasan 1 Tahun Penderita Karsinoma Paru Bukan Sel Kecil Stadium IIIB/IV Usia Lanjut yang Menjalani Kemoterapi Dibandingkan dengan Non Kemoterapi. J Chest Crit Emerg Med. 2015;2:59.
5. Kogure Y, Saka H, Oki M, Saito TI, Ahmed SNM, Kitagawa C, et al. Post-progression survival after EGFR-TKI for advanced non-small cell lung cancer harboring EGFR mutations. PLoS One. 2015;10, e0135393.
6. Nishino M, Dahlberg SE, Cardarella S, Jackman DM, Rabin MS, Ramaiya NH, et al. Volumetric tumor growth in advanced non-small cell lung cancer patients with EGFR mutations during EGFR-tyrosine kinase inhibitor therapy: Developing criteria to continue therapy beyond RECIST progression. Cancer. 2013;119:3761–8.
7. Carney DN, Minna JD. Small cell cancer of the lung. Clin Chest Med. 1982;3:389.
8. Schachter SC, Shafer PO, Sirven JI. Important information on Gefitinib. https://www.epilepsy.com/learn/triggers-seizures/missed-medicines [28.05.16].
9. Wheatley-Price P, Frances A, Shepherd. Epidermal growth factor receptor inhibitors in the treatment of non-small cell lung cancer. In: Stewart DJ, editor. Lung cancer: prevention, management, and emerging therapies. Springer Science & Business Media; 2010. p. 538.
10. Jayanti E, Hakim AR, Indrayuda P. Evaluasi Penggunaan Kemoterapi Pada Pasien Kanker Paru Di Instalasi Rawat Inap RS «X». Universitas Muhammadiyah Surakarta; 2013.

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