Research Articles

Observational Study of Paclitaxel-Carboplatin versus Pemetrexed-Carboplatin for Advanced Pulmonary Adenocarcinoma at Referral Hospital in Jakarta

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Abstract

Platinum-based chemotherapy regimens with two types of drugs, such as paclitaxel-carboplatin and pemetrexed-carboplatin, are first-line therapy for pulmonary adenocarcinoma patients with negative epidermal growth factor receptor (EGFR) mutation. This study aimed to determine the efficacy, toxicity, and cost profile of paclitaxel-carboplatin compared to pemetrexed-carboplatin. This is a cross-sectional study. Pulmonary adenocarcinoma negative EGFR mutation naïve patients treated with paclitaxel-carboplatin or pemetrexed-carboplatin were included. Effectiveness was assessed based on the overall response rate (ORR) according to the response evaluation criteria in solid tumours (RECIST). A pharmacoeconomic analysis is performed based on clinical outcomes consisting of effectiveness and direct medical costs. Medical records from 21 patients with paclitaxel-carboplatin and 21 patients with pemetrexed-carboplatin were successfully evaluated. The effectiveness of the two chemotherapy regimens was not significantly different (OR, 1.25; 95% confidence interval, 0.34 to 4.64; p = 0.739). Frequent haematological toxicities experienced in the two groups were grade 1-2 anaemia, neutropenia, leukopenia. Grade 3 anaemia, leukopenia, and neutropenia were more common in the paclitaxel-carboplatin group. The two groups' nonhematological toxicities were nausea vomitus and hair loss, with peripheral neuropathy more experienced by the paclitaxel-carboplatin group. Cost-minimization analysis reveals that the average cost per patient with pulmonary adenocarcinoma negative EGFR mutation with paclitaxel-carboplatin regimen was cheaper IDR 10,986,257.55 or 50.25%, compared to pemetrexed-carboplatin. In conclusion, there was no significant difference in the effectiveness of the two regimens. The most common adverse effects in both regimens were haematological toxicities. The average cost per patient with a paclitaxel-carboplatin regimen was cheaper compared to pemetrexed-carboplatin.
Keywords: *lung neoplasms, drug therapy, chemotherapy cost, safety.*

Studi Observasi Paclitaxel-Carboplatin versus Pemetrexed-Carboplatin untuk Terapi Adenokarsinoma Paru Lanjut di Rumah Sakit Rujukan di Jakarta

Abstrak

Regimen kemoterapi berbasis platinum dengan dua jenis obat seperti paklitaksel-karboplatin dan pemetreksat-karboplatin merupakan terapi lini pertama pada pasien adenokarsinoma paru dengan mutasi EGFR negatif. Studi ini bertujuan untuk mengetahui profil efikasi, toksisitas, dan biaya paklitaksel-karboplatin dibandingkan pemetreksat-karboplatin. Desain penelitian adalah potong lintang dengan kriteria inklusi pasien adenokarsinoma paru mutasi EGFR negatif yang pertama kali didiagnosis dan diterapi dengan paklitaksel-karboplatin atau pemetreksat-karboplatin. Efektivitas ditentukan berdasarkan ORR menurut kriteria response evaluation criteria in solid tumours (RECIST). Analisis farmakoekonomi dilakukan berdasarkan luaran klinis yaitu efektivitas dan biaya medis langsung. Data berasal dari rekam medis 21 pasien dengan paklitaksel-karboplatin dan 21 pasien dengan pemetreksat-karboplatin. Efektivitas kedua regimen kemoterapi tidak berbeda bermakna (OR 1,25; 95% interval kepercayaan 0,34-4,64; p=0,739). Toksisitas hematologi yang sering dialami oleh kedua kelompok adalah anemia derajat 1-2, neutropenia, leukopenia. Anemia derajat 3, leukopenia, dan neutropenia lebih sering terjadi pada kelompok paklitaksel-karboplatin. Toksisitas nonhematologi kedua kelompok adalah mual, muntah, rambut rontok, dengan neuropati perifer lebih banyak pada kelompok paklitaksel-karboplatin. Dari analisis minimalisasi biaya diketahui biaya rerata pasien dengan regimen paklitaksel-karboplatin lebih murah Rp10.986.257,55 (50,25%), dibandingkan pemetreksat-karboplatin. Disimpulkan bahwa efektivitas kedua regimen tidak berbeda bermakna. Efek samping paling sering adalah toksisitas hematologi dan biaya rerata per pasien dengan regimen paklitaksel-karboplatin lebih murah dibandingkan pemetreksat-karboplatin.
Kata kunci: *neoplasma paru, terapi obat, biaya kemoterapi, keamanan.*

Introduction

Lung cancer is one type of cancer that is getting more and more sufferers. World Health Organization (WHO) estimates that the number of sufferers will increase by 78% in 2025.[1] In Persahabatan Hospital Jakarta, lung cancer patients have jumped fivefold in the last 15 years, from 273 people in 2000 to 1,355 people in 2014.[2] Many patients were already in an advanced stage, causing a poor prognosis.[2,3]

The most common lung cancer is non-small cell lung cancer (NSCLC), with the most type is adenocarcinoma (80-85%) of all lung cancer cases.[4-6] Currently, platinum-based doublet chemotherapy regimens are generally used as first-line therapy in NSCLC patients with negative EGFR mutation.[2,7] Many studies compared the efficacy of various platinum-based doublet chemotherapy regimens in NSCLC patients, however no one specifically has better efficacy than others.[4] Syahruddin et al[3] reported that the use of combination of paclitaxel with carboplatin showed no difference in efficacy and safety compared with other chemotherapy regimens in advanced-stage NSCLC patients. Unfortunately, among many studies, there is no clinical trial that compares directly between paclitaxel-carboplatin with pemetrexed-carboplatin.

Paclitaxel was approved by the Food and Drug Administration (FDA) in 1999, while pemetrexed was approved in 2004. Both drugs are guaranteed funding by the national health insurance in Indonesia, where the price of paclitaxel is cheaper than pemetrexed. In selecting chemotherapy regimen besides the efficacy factor, the cost/ price factor is an important consideration. A pharmacoeconomic study method is needed to analyze clinical factors (efficacy) and economic factors (cost) between the two chemotherapy regimens so patients can get a better quality of life and prevent further waste of cost. This study aims to compare paclitaxel-carboplatin with pemetrexed-carboplatin chemotherapy regimens in Persahabatan Hospital, Indonesia.

Methods

Study Design and Patients

This is a retrospective study with a cross-sectional design using medical record data on pulmonary adenocarcinoma with negative epidermal growth factor receptor (EGFR) mutation patients treated during 2017, April 1st – 2018, December 31st at Persahabatan Hospital (National Respiratory Referral Hospital) in Indonesia. Ethical clearance was obtained with no. 70/KEPK-RSUPP/11/2018. This study used total sampling. The first group of study subjects was all patients with pulmonary adenocarcinoma negative EGFR mutation who received paclitaxel-carboplatin, while the second group was all patients who received pemetrexed-carboplatin chemotherapy. The inclusion criteria were patient aged ≥18 years and confirmed cytology/histology diagnosis of pulmonary adenocarcinoma negative EGFR mutation. The patient had never received chemotherapy before and received paclitaxel 175 mg/m2-carboplatin area under the curve (AUC) five or pemetrexed 500 mg/m2-carboplatin AUC five. The regimen was given every three weeks, at least two cycles must be administered and objective responses was recorded according to response evaluation criteria in solid tumours (RECIST). RECIST criteria consist of complete response, partial response, stable disease, and progressive disease by physical examination and computed tomography (CT) scan thorax contrast examination. All toxicity (haematological and nonhematological) was recorded as well as medical and financial record data for chemotherapy. Patients with incomplete medical and financial records data that can not be evaluated were excluded.

Costs and Cost Perspective

The pharmacoeconomic study was conducted from a provider perspective, national health insurance in Indonesia; hence, only direct medical costs were included. Direct medical costs are costs directly related to the patient's chemotherapy while in the hospital. Direct medical costs consist of drug costs, doctor consultation fees, nurse service costs, use of hospital facilities (inpatient rooms, one daycare, medical device), laboratory costs, costs of diagnosing and treating toxicity that occurs, and the cost of hospitalization due to toxicity chemotherapy.

Outcome Measurements

Effectiveness of therapy was judged by overall response rate (ORR) using RECIST criteria. Complete response (CR) if the tumour evaluation disappears 100%, partial response (PR) if there is a reduction in tumour size of more than 50%, but less than 100% and no new lesions are found. Stable disease (SD) if the tumour size has not changed or shrink more than 25% and less than 50% and no new lesions are found. Progressive disease (PD) if there is an increase in tumour size of more than

25%, or new lesions appear in the lungs or other places. ORR was calculated from the percentage of patients with RECIST results in CR plus PR.

Economic Evaluation

Pharmacoeconomic study with cost-effectiveness analysis method is carried out when clinical outcome of chemotherapy regimens for management pulmonary adenocarcinoma negative EGFR mutation with paclitaxel-carboplatin or pemetrexed-carboplatin give different results. However, if the two regimens mentioned above give the same, similar results, or equivalent, a pharmacoeconomic study will be conducted using the cost-minimization analysis (CMA) method. The calculation is as follow.

$$\frac{\text{Average costs pemetrexed-carboplatin} - \text{average costs paclitaxel-carboplatin}}{\text{average costs pemetrexed-carboplatin}} \times 100\%$$

Statistical Analysis

Patient's characteristics data was presented with descriptive statistics. Bivariate analysis was used to assess differences in the effectiveness of therapy based on ORR using the chi-square test or Fisher's Exact Test. Quantitative data has been collected, processed and analyzed using SPSS version 20.0 (SPSS, Chicago, IL, USA).

Re*sults*

General Characteristics

From medical record data Persahabatan Hospital, a total of 42 patients were found to receive paclitaxel-carboplatin and pemetrexed-carboplatin during the period April 2017 to December 2018. Twenty-one (50%) patients who used paclitaxel-carboplatin was determined as the first group and 21 (50%) patients used pemetrexed-carboplatin as the second group (Figure 1). The characteristics of sex and age are not much different between the two groups. An overview of the basic characteristics of patients can be seen in Table 1.

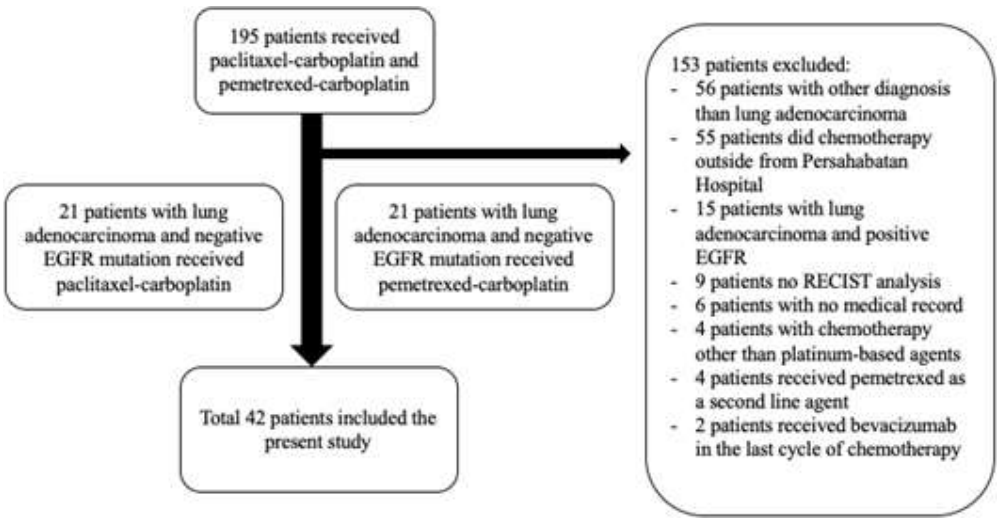

Figure 1. The Flow of Research Subject Selection

Table 1. Characteristics of the Patients

Characteristics	Paclitaxel-Carboplatin n (%)	Pemetrexed-Carboplatin n (%)
Sex		
Male	13 (61.9)	14 (66.7)
Female	8 (38.1)	7 (33.3)
Age (mean ± SD)	52.48 ± 9.9	57.1 ± 11.8
Smoking history		
Non-smoking	10 (47.6)	8 (38.1)
Smoking	11 (52.4)	13 (61.9)
Performance status (PS)		
PS 0	9 (42.9)	5 (23.8)
PS 1	8 (38.1)	15 (71.4)
PS 2	4 (19)	1 (4.8)
Chemotherapy cycle		
2 cycles	0 (0)	1 (4.8)
3 cycles	2 (9.5)	1 (4.8)
4 cycles	3 (14.3)	1 (4.8)
5 cycles	2 (9.5)	4 (19)
6 cycles	14 (66.7)	14 (66.7)
Stage		
IIIA	4 (19)	2 (9.5)
IIIB	5 (23.8)	4 (19)
IV	12 (57.1)	15 (71.4)
Health insurance		
NHI	21 (100)	21 (100)
Private	0 (0)	0 (0)

Effectiveness Analysis

The effectiveness of chemotherapy is determined by the ORR, which is the percentage of patients with RECIST complete response plus PR. Most treatment responses were SD with 25 patients (59.5%), PR 13 patients (31%), PD 4 patients (9.5%). No patient experienced CR in the 2 regimens. In the first group, there were 13 SD patients (61.9%), 6 PR patients (28.6%), 2 PD patients (9.5%), so the first group ORR was 28.6%. In the second group, SD was obtained by 12 patients (57.1%), PR 7 patients (33.3%), PD 2 patients (9.5%), so the second group's ORR was 33.3%. There were no significant different (chi-square test, p = 0.739) between the 2 regimens, thus the regimens had the same effectiveness (Table 2).

Table 2. The Effectiveness of Therapy Based on Overall Response Rate

Chemotherapy Regimen	Effectiveness		OR (95% CI)	p value
	Yes n (%)	No n (%)		
Paclitaxel-Carboplatin	6 (28.6)	15 (71.4)	1.25 (0.337 – 4.639)	0.739
Pemetrexed-Carboplatin	7 (33.3)	14 (66.7)		

Safety Analysis

Chemotherapy toxicity is a complaint or symptom that results from the side effects of a chemotherapy regimen. This study divides haematological toxicity between the form of anaemia, leukopenia, neutropenia, and thrombocytopenia with a grade of toxicity following WHO classification, namely grade 0 (no toxicity), grade 1-2 (mild toxicity), and grade 3-4 (severe toxicity). Generally, patients in both groups did not experience toxicity (grade 0), and no

severe toxicity grade was found (grade 4). Grade 1-2 anaemia, neutropenia, and leukopenia are the most frequent haematological toxicity experienced by both groups. For grade 3, anaemia, leukopenia, and neutropenia are mostly experienced by the first group. Nonhematological toxicity like nausea, vomiting, hair loss, diarrhoea, myalgia, and peripheral neuropathy was found in both groups. Both groups experienced nausea, vomiting, and alopecia. Peripheral neuropathy is more common in the first group. Complete data on nonhematological toxicity can be seen in Table 3.

Cost Analysis

From 42 patients, there were 185 cycles of chemotherapy conducted at ODC; the first group had 97 cycles and the second group had 88 cycles. The cost of chemotherapy in one daycare (ODC) room Persahabatan hospital consists of laboratory examination costs, hospital administration, doctor service, chemotherapy package costs set by NHI (consist of ODC accommodation costs, doctor visits, infusion, injection, oximeter pulse installations, and cytostatics), paclitaxel-carboplatin or pemetrexed -carboplatin regimen, CT scan thorax contrast, premedication, and medicine to take home).

Chemotherapy package costs from NHI was 2,000,000 Indonesian Rupiah (IDR) for every patient. The price of chemotherapy package components was ODC accommodation 600,000 IDR, oximeter pulse installations 150,000 IDR, and cytostatics 930,000 IDR. For laboratory costs, hospital administration, doctor service, paclitaxel-carboplatin or pemetrexed-carboplatin regimen, CT scan thorax contrast, and other costs (premedication, medicine to take home) claimed to the NHI separated from chemotherapy package costs.

Laboratory examination costs were carried out by the standard operating procedure established by ODC chemotherapy. Before being given chemotherapy each cycle, every patient, must be examined for complete blood (routine blood, type count, sedimentation rate), liver function (alanine transaminase, aspartate aminotransferase), glucose at random, electrolyte packets (sodium, potassium, chloride), and kidney function (ureum, creatinine).

The cost of the paclitaxel-carboplatin and pemetrexed-carboplatin regimen can vary and differ for each patient and each cycle, depend on the availability of the regimen in the pharmacy department. Premedication drugs were given before chemotherapy consist of dexamethasone injection, diphenhydramine, ranitidine, and ondansetron 4 mg injection. Prescription medications to take home are mefenamic acid, ondansetron, ranitidine, B complex vitamine, and blood-booster tablet with different prices, quantities, and types depend on the patient's situation and condition.

Chemotherapy ODC costs and their cost components are shown in Table 4. Patients who experience severe haematological and nonhematological toxicity were advised to be hospitalized for transfusion, reduce complaints, and improve general condition. From the first group, ten patients were admitted related to toxicity with a total frequency of hospitalization 20 times, range of hospitalization 1-8 days, and 7 of them underwent chemotherapy for a total of 15 cycles. From the second group, 11 patients were hospitalized related to toxicity with a total frequency of hospitalization 30 times, range of hospitalization 1-19 days and all underwent chemotherapy as much 25 cycles.

Hospitalization costs include hospital administration, medical expense, doctor visits, accommodation (VIP-class III), health support (clinical laboratories, blood banks, radio-diagnostics), medical device, inpatient drugs out of chemotherapy and chemotherapy.

The effectiveness of paclitaxel-carboplatin and pemetrexed-carboplatin is equivalent (Table 2). Therefore, a pharmacoeconomic study was conducted with a cost-minimization analysis (CMA) method. The CMA calculation is as follows: the total cost of chemotherapy and toxicity per patient with the paclitaxel-carboplatin regimen was 10,878,804.6 IDR, while the total cost of chemotherapy and toxicity per patient with the pemetrexed-carboplatin regimen was 21,865,062.15 IDR. Thus, the average cost per patient for negative EGFR mutation pulmonary adenocarcinoma with the paclitaxel-carboplatin regimen was cheaper 10,986,257.55 IDR or 50.25% to the pemetrexed-carboplatin regimen.

$$\frac{(Rp\ 7.265.702{,}95 + Rp\ 14.599.359{,}2) - (Rp\ 4.257.945{,}48 + Rp\ 6.620.859{,}1)}{Rp\ 7.265.702{,}95 + Rp\ 14.599.359{,}2} \times 100\% = 50{,}25\%$$

Table 3. Hematological and Non-hematological Toxicities

Variables	Paclitaxel-Carboplatin n (%)	Pemetrexed-Carboplatin n (%)
Anemia		
Grade 0	9 (42.9)	2 (9.5)
Grade 1-2	10 (47.6)	18 (85.7)
Grade 3-4	2 (9.5)	1 (4.8)
Leucopenia		
Grade 0	14 (66.7)	16 (76.2)
Grade 1-2	6 (28.6)	5 (23.8)
Grade 3-4	1 (4.8)	0 (0)
Neutropenia		
Grade 0	11 (52.4)	14 (66.7)
Grade 1-2	8 (38.1)	6 (28.6)
Grade 3-4	2 (9.5)	1 (4.8)
Thrombocytopenia		
Grade 0	19 (90.5)	18 (85.7)
Grade 1-2	2 (9.5)	3 (14.3)
Grade 3-4	0 (0)	0 (0)
Nausea and vomiting		
No	6 (28.6)	8 (38.1)
Yes	15 (71.4)	13 (61.9)
Hair loss		
No	19 (90.5)	18 (85.7)
Yes	2 (9.5)	3 (14.3)
Diarrhea		
No	6 (28.6)	8 (38.1)
Yes	15 (71.4)	13 (61.9)
Myalgia		
No	19 (90.5)	20 (95.2)
Yes	2 (9.5)	1 (4.8)
Peripheral neuropathy		
No	14 (66.7)	20 (95.2)
Yes	7 (33.3)	1 (4.8)

Table 4. Cost Components of Chemotherapy in One Day Care

Average Cost Component	Paclitaxel-Carboplatin IDR	Pemetrexed-Carboplatin IDR
Laboratory	1,404,190.48	1,244,952.38
Hospital administration	151,428.57	131,428.57
Doctor consul service	101,619.05	89,047.62
ODC accommodation	2,771,428.57	2,428,571.43
Doctor visits	923,809.52	809,523.81
Infusion	277,142.86	242,857.14
Injection	277,142.86	242,857.14
Oximeter pulse	692,857.14	607,142.86
Cytostatic	4,295,714.29	3,764,285.71
Paclitaxel/Pemetrexed	6,232,858.57	25,547,971.4
Carboplatin	2,386,530.29	2,059,742.76
Other costs	200,490.81	132,777.71
CT scan thorax contrast	3,257,142.86	3,500,000
Average total	22,972,355.9	40,801,158.6
Average total/cycle	89,416,855	152,579,762
Average total/cycle/patient	4,257,945.48	7,265,702.95

Discussion

This study found that the effectiveness of therapy based on ORR between the two groups was not significantly different. The result of this study consistent with previous studies conducted by Schiller et al[9] which compared four chemotherapy regimens, paclitaxel-cisplatin, gemcitabine-cisplatin, docetaxel-cisplatin, and paclitaxel-carboplatin in 1155 advanced-stage NSCLC patients. The ORR did not differ significantly between the four chemotherapy regimens (ORR 21%; 22%; 17%; and 17%). Another study in Italy by Scagliotti et al[10] comparing gemcitabine-cisplatin, paclitaxel-carboplatin, vinorelbine-cisplatin in advanced stage NSCLC patients also found that ORR did not significantly different (ORR 30%; 32%; 30%). The same result was obtained in a study conducted by Ohe et al.[11] in Japan in 602 advanced-stage NSCLC patients but with different regimens, namely irinotecan-cisplatin, paclitaxel-carboplatin, gemcitabine-cisplatin, and vinorelbine-cisplatin. No significant different in ORR (ORR 31%; 32.4%; 30.1%; 33.1%) or overall survival and all four regimens were well tolerated. Syahruddin et al[3] reported that the use of combination paclitaxel with carboplatin had no difference in the efficacy and safety compared with other chemotherapy regimens such as combination docetaxel, gemcitabine, vinorelbine with platinum in advanced stage NSCLC patients. Therefore, the combination of paclitaxel-carboplatin and pemetrexed-carboplatin can be used interchangeably in advanced pulmonary adenocarcinoma patients.

The frequent haematological toxicity in the two groups was the same, namely grade 1-2 anaemia, neutropenia, leukopenia, and thrombocytopenia. Nonhematological toxicities that were often experienced by both groups were nausea-vomiting and hair loss. Peripheral neuropathy was more common in the paclitaxel-carboplatin group. The pemetrexed-carboplatin group with a heavier performance status (the majority of PS 1) experienced less toxicity when compared to the paclitaxel-carboplatin group, whose performance status was generally lighter (the majority of PS 0). All patients, although undergo toxicity, continued the chemotherapy regimens after the toxicities were resolved.

Study by Laohavinij et al[12] in Thailand involving 53 patients with advanced stages NSCLS, the most common toxicities were grade 3-4 granulocytopenia (25%), anaemia (3%), thrombocytopenia (1%), neutropenic fever (1.5%), angina pectoris (1%) and anaphylaxis (0.4%). Other generally mild toxicity, including myalgia, arthralgia, peripheral neuropathy, and asthenia. Ohe et al[11] in Japan in 148 advanced-stage NSCLC patients with frequent haematological toxicities were grade 2 anaemia (42%), grade 2 leukopenia (39%), for nonhematological toxicity were grade 2 alopecia (45%), grade 2 constipation (39%), arthralgia (20%), and grade 2 sensory neuropathy (14%). Study by Langer et al [13] with 54 NSCLC patients found that 70% of patients had grade 3 or 4 granulocytopenia after the first cycle with granulocyte colony-stimulating factor this incidence decreased in the next cycle to reach <20%, grade 3 or 4 toxicity others were thrombocytopenia (13%), anaemia (9%), fatigue (9%), neutropenic fever (5%), and cystitis bleeding (1%). Jhonson et al[14] demonstrated that in 51 NSCLC patients with stage IIIB or IV found hematological toxicity was grade 3 or 4 granulocytopenia and thrombocytopenia, while nonhematological toxicity was nausea, vomiting, neuropathy, arthralgia/myalgia.

Kosmidis et al[15] found that the most haematological toxicity in 55 inoperable advanced stages NSCLC patients were grade 2/3 neutropenia (14%), grade 3/4 thrombocytopenia (4%), nonhematological toxicities were grade 2/3 alopecia (59%), neurotoxicity (3%), myalgia/ arthralgia (10%). Research about pemetrexed-carboplatin toxicity, include Scagliotti et al[16] in 39 advanced stages NSCLC patients found that the most common haematological toxicities were grade 3 neutropenia 6 (15,4%) patients, grade 3 thrombocytopenia 6 (15,4%) patients, and grade 3 anaemia 3 (7,7%) patients. Nonhematological toxicity were grade 3 fatigue 3 (7,7%) patients, grade 3 stomatitis 1 (2,6%), and grade 3 neutropenia fever 1 (2,6%) patients.

Zinner et al[17] reported out of 50 advanced stages NSCLC patients were 27 (54%) had grade 1 anemia, 22 (44%) had grade 1 thrombocytopenia, 27 (54%) with grade 2 nausea, and grade 1 alopecia 24 (48%) patients. Gronberg et al[18] reported that in advanced-stage NSCLC patients the most frequent hematological toxicities were grade 3 granusitopenia in 52 (25%) patients, grade 3 leukopenia in 37 (18%), grade 3 thrombocytopenia in 28 (13%), and grade 3 anemia in 25 (12%) patients.

The results of haematological and nonhematological toxicities of this study are almost the same as previous studies, only slightly different in the grade of toxicities, wherein foreign studies,

there is a more severe grade of toxicity which can be caused by the large dosage of the regimen used and differences in race and genetic in subjects research.

Under the Guidelines for Diagnosis and Management of Lung Cancer in Indonesia issued by the Association of Indonesian Lung Doctors regarding the principle of choosing an anticancer type and administering a chemotherapy regimen is an objective response to an anticancer drug 15%, the toxicity of the drug does not exceed grade 3 WHO scale.[5] The present study results shows that both from the effectiveness of therapy and toxicity, paclitaxel-carboplatin regimen and pemetrexed-carboplatin can be used as a chemotherapy option because the objective response is >15% and the toxicity does not exceed grade 3 WHO scale.

The effectiveness of paclitaxel-carboplatin and pemetrexed-carboplatin is the same or equivalent, thus a pharmacoeconomic study using a CMA method is obtained. The average cost per patient pulmonary adenocarcinoma negative EGFR mutation with the paclitaxel-carboplatin regimen is cheaper 10,986,257.55 rupiah (50.25%) compared to the pemetrexed-carboplatin regimen. Pemetrexed regimen was still in the patent period so the price was expensive and there were differences in inpatient facility between the two groups.

The limitations of this study are this research is a preliminary study considering that lung cancer cases have many choices of combination chemotherapy regimens. This study uses a retrospective method with a limited number of patients in one hospital so the results of pharmacoeconomic studies with a cost-minimization analysis method only apply to these hospitals and cannot be generalized in a hospital or other health care center.

Conclusion

Based on pharmacoeconomic study using the AMiB method, paclitaxel-carboplatin regimens are 50.25% cheaper than the pemetrexed regimen. However, this study supports the use of a combination of platinum-based chemotherapy with third-generation cytotoxic drugs. There was no significant difference between the combination of carboplatin-paclitaxel and carboplatin-pemetrexed in terms of efficacy as well as side effects, therefore the two chemotherapy combinations could be used interchangeably.

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