RESEARCH ARTICLE

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Survival Analysis and Clinical Outcomes between Paclitaxel and Carboplatin Versus Carboplatin and Gemcitabine in Patients with Advanced-stage Non-small-cell Lung Cancer: A Single-center Cohort Study

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Abstract

Background: Palliative chemotherapy using platinum-based doublet chemotherapy was recommended as one of the standard treatments in patients with advanced-stage non-small cell lung cancer (NSCLC) with negative EGFR mutation. This study aimed to compare clinical outcomes between patients treated with paclitaxel and carboplatin (PC) and those treated with carboplatin and gemcitabine (CG). **Methods:** We conducted a retrospective cohort study comparing PC and CG at Hatyai Hospital between 2012 and 2019. The primary outcome was survival analysis, and the secondary outcome was chemotherapy-related adverse events, and the rate and reason for stopping chemotherapy. **Result:** The median overall survivals of both groups was comparable (9.0 months for the PC group and 9.6 months for the CG group; log-rank, p=0.287). The CG group had a higher incidence of adverse events (89.7% vs. 77.9%, p=0.010) and tended to have a lower rate of chemotherapy discontinuation (29.6% vs. 41.2%, p=0.080) than the PC group. In the multivariate analysis, female sex (odds ratio [OR]=0.351; 95% confidence interval [CI], 0.158-0.780; p=0.010) and higher performance status (OR=76.374; 95%CI, 32.533-179.295; p<0.001) were independent predictive factors for stopping chemotherapy. In the proportional hazards model, the factors associated with decreased survival included higher performance status (hazard ratio [HR]=1.939; 95%CI, 1.388-2.709; P<0.001) and discontinuation of chemotherapy (HR=2.572; 95%CI, 1.792-3.691; p=<0.001). **Conclusion:** These two platinum-based regimens had comparable effects on overall survival. The CG group had a higher incidence of chemotherapy-related adverse events, while the PC group had a marginally significantly higher rate of stopping chemotherapy from unacceptable adverse events and deterioration of patients' clinical status.

Keywords: non-small cell lung cancer- chemotherapy- wild type EGFR- platinum-based doublet chemotherapy

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Introduction

Lung cancer is the leading cause of cancer-related death worldwide. This burden results from most patients having an advanced stage at the time of diagnosis, resulting in a 5-year survival rate of < 10% (Walling, 1994). Previously, a large population-based real-world study demonstrated the median overall survival (OS) in patients with stage IV non-small cell lung cancer (NSCLC) without known EGFR mutation, or anaplastic lymphoma kinase rearrangement was 9.7 months, varying from 8.5 to 10.0 months depending on pathological cell type (Abernethy et al., 2017).

In patients with advanced-stage NSCLC, the treatment options are palliative chemotherapy, targeted therapy, immune checkpoint inhibitors, and supportive treatment. In general, treatment decisions depend on the patients' clinical status, comorbidities, biomarkers, and affordability.

The recommendation of clinical practice guidelines is based on data from clinical trials conducted in experienced centers in developed countries, which limits their application in general. In real-world practice, multiple factors influencing adherence to guidelines vary depending on medical advancement, national culture, and financial status. In areas where medical resources are limited, palliative chemotherapy with platinum-based

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doublet chemotherapy is one of the standard treatments for patients with advanced-stage NSCLC with negative EGFR mutations (Ettinger et al., 2021).

To date, several studies have failed to demonstrate which specific platinum-based doublet chemotherapy could provide superior efficacy. This study aimed to compare the survival and clinical outcomes of paclitaxel and carboplatin (PC) versus carboplatin and gemcitabine (CG) in patients with advance-stage non-small cell lung cancer who were negative for EGFR.

Materials and Methods

Study design and patient population

This retrospective cohort study was conducted at Hatyai Hospital, a university-affiliated tertiary center in southern Thailand. The study protocol was approved by the Institutional Review Board of Hatyai Hospital (protocol number HYH EC 102-64-01) and conducted in accordance with the Declaration of Helsinki. The inclusion criteria were patients aged > 18 years with advanced-stage NSCLC who were negative for EGFR mutations and received chemotherapy as the first-line treatment between 2012 and 2019. The exclusion criteria were as follows: 1) previous treatment with chemotherapy or any cancer-specific treatment from other hospitals; 2) presence of renal, cerebral, hepatic, and cardiopulmonary dysfunction; and 3) concurrent with other malignancies.

Data collection

We retrospectively reviewed the medical records of all patients. Demographic and clinical variables (including age, sex, histological cell type, performance status, metastasis site, and laboratory results) at the time of diagnosis were collected. We also recorded the number of cycles of chemotherapy, chemotherapy-related adverse events, treatment response, incidence of premature cessation of chemotherapy, and reasons for premature cessation of chemotherapy.

We stratified patients into two groups; a "PC group" that received paclitaxel and carboplatin and a "CG group" treated with carboplatin and gemcitabine as the first line regimen of treatment.

Treatment and evaluation of response

The routine protocol of chemotherapy in each group was as follows: In the PC group, paclitaxel 175 mg/m^2 was infused over three hours accompanied with carboplatin area under the plasma concentration/time curve (AUC) of 5-6 according to Calvert formula (van Warmerdam et al., 1995), infusion over 15–30 min; in the GC group, gemcitabine 1000 mg/m^2 was infused over 30 min accompanied with carboplatin AUC of 5-6 according to Calvert formula, infusion over 15–30 min on day one following another dose of gemcitabine (1000 mg/m^2) on day eight. In the PC group, prophylactic medication, including intravenous dexamethasone 20 mg, diphenhydramine 50 mg, and ranitidine 50 mg, was usually prescribed 1 h before chemotherapy initiation. The following treatment cycles were repeated four weeks after the prior cycle until complete regimens (usually consisting of 4-6 cycles of chemotherapy). Chemotherapy was discontinued in patients who developed unacceptable adverse events or progressive disease. All patients were required to have a performance status ≤ 1 and adequate bone marrow reserve (absolute neutrophil count > 1,500/mm^3 and platelets > 100,000/mm^3).

Outcome and definitions

The primary outcome of this study was OS, which was calculated from the date of diagnosis until either death or the last follow-up date (sensor survival time was 1st January 2022). Secondary outcomes were the rates of chemotherapy-related adverse events and premature discontinuation of treatment regimens. We also evaluated the reasons for the premature discontinuation of chemotherapy.

NSCLC was diagnosed based on histopathology and staged according to the eighth edition lung cancer stage classification (Detterbeck et al., 2017). Patient performance status was determined according to the Eastern Cooperative Oncology Group (ECOG) (Oken et al., 1982). We stratified chemotherapy-related adverse events into two groups (hematologic and non-hematologic adverse events) based on Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (Freites-Martinez et al., 2021). Neutropenia was determined if the absolute neutrophil count was <1500/mm^3, and thrombocytopenia was diagnosed if a platelet count was <100,000/mm^3. Significant anemia was defined as a hemoglobin level less than eight g/dL or requirement for blood transfusion. Infection was determined if the patient had evidence of fever with or without organ-specific symptoms, such as pneumonia, urinary tract infection, intra-abdominal infection, or primary bacteremia. Complete treatment was defined as the patients who received at least four cycles of chemotherapy.

Progressive disease (PD) was defined as an increase in the sum of the longest diameter of the targeted lesion compared with the smallest sum recorded by at least 20%, the appearance of one or more new lesions, or unequivocal progression of non-target lesions, according to the modified Response Evaluation Criteria in Solid Tumors (Nishino et al., 2014). Patients whose chemotherapy was stopped because of PD or death before the next treatment cycle were determined to have stopped chemotherapy due to PD.

Statistical analysis

Categorical variables were presented as frequency statistics and percentages, and were compared using Fisher's exact test. Continuous variables are presented as means with standard deviations or medians with interquartile ranges (IQR) using Student's t-test or Wilcoxon rank-sum test. Survival analyses were performed using the Kaplan–Meier method, and the log-rank test was used to analyze the statistical differences between the study groups.

Logistic regression analyses were used to assess the relationship between prematurely stopping chemotherapy and clinical and biological factors using the following variables: sex, age, pathologic cell type (squamous and

non-squamous), presence of local (including lung, pleura, and pericardium) and distant (including bone, brain, liver, and adrenal) metastasis, ECOG performance status, use of palliative radiation therapy, hemoglobin levels, and serum creatinine levels. The Cox proportional hazards model was used to identify the survival-influencing variables. In both the binary logistic regression and Cox proportional analyses, sex, age, and other variables (p-values <0.1 in the univariate analysis were included in the multivariate analyses. Statistical significance was set at p<0.05. All data analyses were performed using Stata Statistical Software Version 15.1 (StataCorp LLC, College Station, TX, USA).

Results

Baseline characteristics

During the study period, 321 patients were enrolled, with a mean age of 61.6 years, and 223 (69.5%) were male. Of these, 253 patients were classified into the GC group and 68 into the PC group. Comparisons of patient demographic data are presented in Table 1. The proportion of male patients was higher in the GC group than in the PC group, whereas the use of palliative radiation therapy was higher in the PC group than in the GC group. Adenocarcinoma was the most common histologic subtype in both groups.

Adverse events and cycle of chemotherapy

Table 2 shows a comparison of chemotherapy-related adverse events between the two groups. Patients in the CG group developed both hematologic (45.8% vs. 19.1%, p<0.001) and non-hematologic adverse events (85.0% vs. 70.6%, p=0.006) compared to those in the PC group. In the subclassification, the CG group had a higher incidence of neutropenia, significant anemia, nausea/vomiting, and fatigue, while the PC group had a higher rate of sensory neuropathy.

Patients in the CG group tended to receive more cycles of chemotherapy (median [IQR], 4 [3–6] cycles vs. 4 [2–6] cycles, p=0.056), and patients in the PC group tended to have a higher rate of premature discontinuation of chemotherapy (29.6% vs. 41.2%, p=0.080) compared to GC, mainly due to unacceptable adverse events (13.0% vs. 25.0%, p=0.016) and deterioration of performance status (9.1% vs. 19.1%, p=0.020).

Survival analysis

The median OS of the CG and PC groups were 9.6 months and 9.0 months, respectively. Based on the Kaplan–Meier method (Figure 1), the overall survival rate of patients in the PC group was not significantly different from that in the GC group (overall 1-, 2-, and 3-year cumulative survival rates were 38% vs. 33%, 16% vs. 17%, and 8% vs. 6%, respectively; log-rank test, p=0.287) (Table 3).

Predictors for the achievement of prematurely stopping the chemotherapy

Univariate logistic regression analysis revealed that female sex (odds ratio [OR]=0.548; 95% confidence interval [CI], 0.319-0.942; p=0.030), increased hemoglobin levels (OR=0.802; 95%CI, 0.701-0.917; p=0.001), and higher performance status at the time of diagnosis (OR=69.023; 95% CI, 36.607-155.658; p<0.001) were prognostic factors for stopping chemotherapy. The use of the PC regimen was marginally associated with discontinuation of chemotherapy (OR=1.661; 95% CI, 0.955-2.889; p=0.072). In the multivariate analysis, only female sex (OR=0.351; 95% CI, 0.158-0.780; p=0.010)

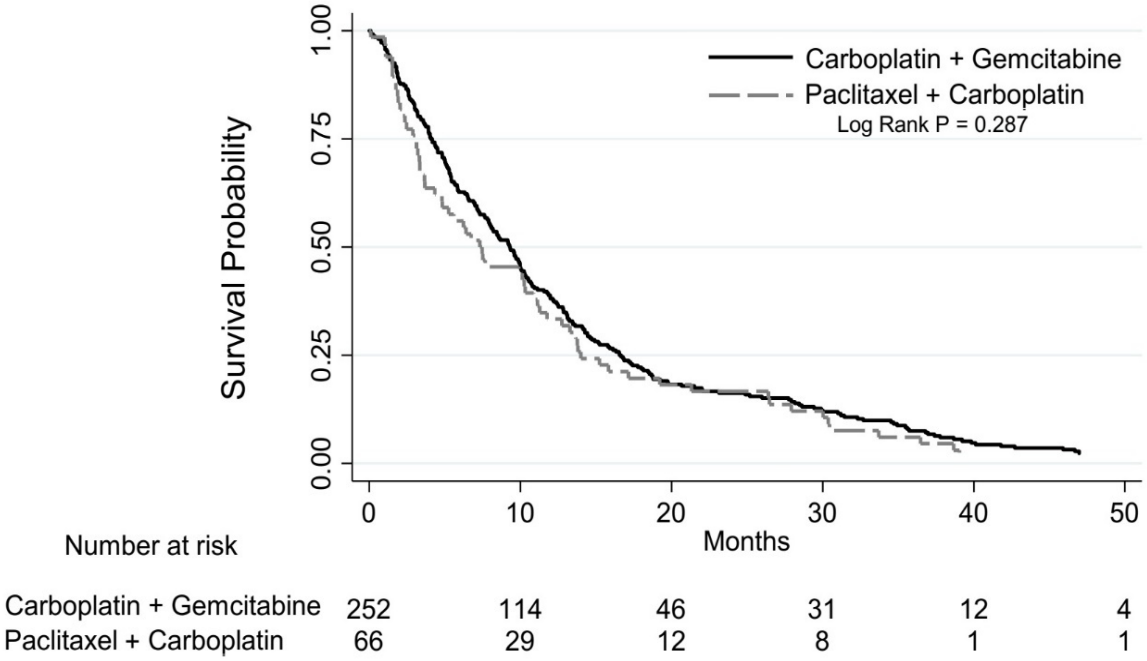

Figure 1. Kaplan-Meier Estimate for Overall Survival of Patients Treated with Carboplatin + Gemcitabine and Paclitaxel + Carboplatin.

Table 1. Demographic Data of the Patients in the Two Groups

	CG group (%) (n=253)	PC group (%) (n=68)	P value
Age (years): mean ±SD	61.7 ± 12.2	60.2 ± 13.4	0.398
Male sex	168 (66.4)	55 (52.9%)	0.021
Histologic cell type			0.219
Adenocarcinoma	189 (74.7)	44 (64.7)	
Squamous	46 (18.2)	16 (23.5)	
Large cell carcinoma	1 (0.4)	0 (0)	
Adeno-squamous	1 (0.4)	0 (0)	
NOS	16 (6.3)	8 (11.8)	
Performance status			0.252
0	157 (62.1)	37 (54.4)	
1	96 (37.9)	31 (45.6)	
Metastasis			
Distant	144 (55.7)	37 (54.4)	0.846
Bone	58 (22.9)	17 (25.4)	0.674
Brain	52 (20.6)	19 (27.9)	0.192
Liver	49 (19.4)	9 (13.2)	0.243
Adrenal	26 (10.3)	10 (14.7)	0.304
Local	177 (70)	47 (69.1)	0.893
Lung	113 (44.7)	33 (48.5)	0.57
Pericardium	18 (7.1)	1 (1.5)	0.089
Pleura	95 (37.5)	24 (35.3)	0.732
Hemoglobin (g/dL): mean ± SD	11.9 ± 1.8	11.5 ± 1.9	0.077
White blood cell (/mm^3): mean ± SD	10170 ± 4282	11083 ± 4836	0.13
Serum creatinine (mg/dL): median (IQR)	0.72 (0.66-0.88)	0.69 (0.60-0.87)	0.32
Palliative radiotherapy	69 (27.3)	30 (44.1)	0.008

CG, carboplatin + gemcitabine; PC, paclitaxel + carboplatin; SD, standard deviation; NOS, not otherwise specified; IQR, interquartile range

Table 2. Toxicity, Tolerability, and Causes of Stopping Chemotherapy According to Treatment Group

Variables	CG group (%) (n=253)	PC group (%) (n=68)	P value
Adverse events	227 (89.7)	53 (77.9)	0.01
Hematologic events	116 (45.8)	13 (19.1)	< 0.001
Neutropenia	52 (20.6)	5 (7.4)	0.011
Thrombocytopenia	28 (11.1)	4 (5.9)	0.205
Anemia	87 (34.4)	6 (8.8)	< 0.001
Non-hematologic events	215 (85.0)	48 (70.6)	0.006
Infection	53 (20.9)	11 (16.2)	0.382
Nausea/vomiting	87 (34.4)	11 (16.2)	0.004
Diarrhea	11 (4.3)	2 (2.9)	1
Sensory neuropathy	13 (5.1)	10 (14.7)	0.014
Alopecia	0 (0)	0 (0)	N/A
Fatigue	173 (68.4)	37 (54.4)	0.032
Cycles of received chemotherapy: median (IQR)	4 (3-6)	4 (2-6)	0.056
Premature discontinuation of chemotherapy	75 (29.6)	28 (41.2)	0.08
Cause of chemotherapy discontinuation			
Total cause	75 (29.6)	28 (41.2)	0.071
Unacceptable side effect	33 (13)	17 (25)	0.016
Progressive disease	21 (8.3)	6 (8.8)	0.89
Poor performance status	23 (9.1)	13 (19.1)	0.02

CG, carboplatin + gemcitabine; PC, paclitaxel + carboplatin; IQR, interquartile range

Table 3. Overall Survival in the Two Groups

	CG group (n=253)	PC group (n=68)
Median survival time, months	9.6	9
1-year survival	38	33
2-year survival	16	17
3-year survival	8	6
4-year survival	2	2
5-year survival	0	0

CG, carboplatin + gemcitabine; PC, paclitaxel + carboplatin

and higher performance status (OR=76.374; 95% CI, 32.533-179.295; p<0.001) were independent prognostic factors for premature discontinuation of chemotherapy (Table 4).

Predictors for overall survival

Cox proportional hazards model analyses were performed to identify the factors affecting OS (Table 5). In the univariate analysis, the factors significantly associated with an elevated mortality risk included increased hemoglobin levels (hazard ratio [HR]=0.928; 95%CI, 0.867-0.994; p=0.034), higher performance status (HR=3.324; 95%CI, 2.627-4.206; p<0.001), and premature discontinuation of chemotherapy (HR=4.122; 95% CI, 3.218-5.280; p<0.001). In the multivariate analysis, higher performance status (HR=1.939; 95% CI, 1.388-2.709; p<0.001) and premature discontinuation of chemotherapy (HR=2.572; 95% CI, 1.792-3.691; p<0.001) were independently associated with decreased OS.

Discussion

Several studies have shown the benefits of platinum-based chemotherapy on the OS of patients with advanced-stage lung cancer with negative EGFR mutations (Zhu et al., 2013; Lee et al., 2014; Tomasini et al., 2017). However, data identifying better platinum-based doublet regimens remains limited. To answer this question, we conducted a cohort study comparing the clinical outcomes of advanced-stage lung cancer patients who received CG and PC. The main results of this study are as follows. First, there was no statistically significant difference in OS between patients treated with CG and PC regimens. Second, even though there was a

Table 4. Univariate and Multivariate Logistic Regression Analysis of Factors Predictive of Premature Discontinuation of Chemotherapy

Factors	Univariate		Multivariate	
	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Age, every 1 unit increased	1.001 (0.982–1.020)	0.908	0.995 (0.967–1.024)	0.074
Female sex	0.548 (0.319–0.942)	0.03	0.351 (0.158–0.780)	0.01
Age > 60 yrs	1.179 (0.735–1.891)	0.494		
Histology		0.974		
Non-squamous	1 (reference)			
Squamous	1.010 (0.558–1.827)			
Metastasis				
Distant	1.053 (0.657–1.688)	0.831		
Bone	0.773 (0.437–1.366)	0.376		
Brain	1.018 (0.508–1.788)	0.952		
Liver	0.942 (0.510–1.740)	0.85		
Adrenal	0.794 (0.368–1.715)	0.557		
Local	0.723 (0.438–1.194)	0.205		
Lung	0.848 (0.529–1.360)	0.949		
Pericardium	0.547 (0.177–1.691)	0.295		
Pleura	0.930 (0.517–1.513)	0.77		
ECOG		<0.001		<0.001
0	1 (reference)		1 (reference)	
1	69.023 (36.607–155.658)		76.374 (32.533–179.295)	
Chemotherapy		0.072		0.321
CG	1 (reference)		1 (reference)	
PC	1.661 (0.955–2.889)		1.562 (0.647–3.771)	
Hemoglobin, every 1 unit increased	0.802 (0.701–0.917)	0.001	0.922 (0.761–1.116)	0.405
Creatinine, every 1 unit increased	0.714 (0.319–1.600)	0.413		
Palliative radiotherapy	0.829 (0.455–1.387)	0.474		

CG, carboplatin + gemcitabine; PC, paclitaxel + carboplatin; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group

Table 5. Univariate and Multivariate Logistic Regression Analysis of Factors Predictive of Overall Survival

Factors	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age, every 1 unit increased	1.000(0.991–1.009)	0.986	1.001 (0.992–1.011)	0.804
Female sex	0.821 (0.645–1.045)	0.109	0.997 (0.773–1.288)	0.984
Age > 60 yrs	0.958(0.767–1.196)	0.702		
Histology		0.323		
Non-squamous	1 (reference)			
Squamous	1.152 (0.870–1.524)			
Type of metastasis				
Distant	1.027 (0.823–1.283)	0.812		
Bone	0.817 (0.629–1.063)	0.133		
Brain	1.206 (0.922–1.578)	0.172		
Liver	1.229 (0.918–1.644)	0.166		
Adrenal	0.936 (0.611–1.326)	0.709		
Local	0.987 (0.773–1.261)	0.918		
Lung	0.953 (0.763–1.191)	0.672		
Pericardium	0.911 (0.573–1.449)	0.694		
Pleura	1.132 (0.899–1.425)	0.292		
ECOG		<0.001		<0.001
0	1 (reference)		1 (reference)	
1	3.324 (2.627-4.206)		1.939 (1.388–2.709)	
Hemoglobin, every 1 unit increased	0.928 (0.867–0.994)	0.034	1.016 (0.949–1.087)	0.65
Creatinine, every 1 unit increased	0.890 (0.691–1.147)	0.369		
Premature discontinuation of chemotherapy	4.122 (3.218–5.280)	<0.001	2.572 (1.792–3.691)	<0.001
Palliative radiotherapy	0.910 (0.716–1.156)	0.438		
Type of chemotherapy		0.288		
CG	1 (reference)			
PC	1.159 (0.883–1.521)			

HR, hazard ratio; CG, carboplatin + gemcitabine; PC, paclitaxel + carboplatin; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group

higher rate of chemotherapy-related adverse events in the CG regimen, patients who received this regimen tended to receive more cycles of chemotherapy and tended to prematurely discontinue chemotherapy less than those treated with the PC regimen. Third, female sex and poorer performance status were associated with premature discontinuation of chemotherapy. Finally, higher performance status and premature discontinuation of chemotherapy were independent positive factors for decreased OS.

Our study demonstrated real-world data on the management of patients with advanced-stage NSCLC with negative EGFR mutations, and was conducted in a regional referral center in Thailand, where medical resources were limited. Patients in our center were treated according to evidence-based guidelines, followed by a reimbursement process through the nationally publicly funded health care system. In our practice, carboplatin (as platinum-based chemotherapy) is preferred because of its lower toxicity profile (including nausea, vomiting, neutropenia, renal impairment, neurotoxicity, and alopecia) compared to the cisplatin-based regimen (Moro-Sibilot et al., 2015).

OS of patients in this study was not significantly different between the two groups, which is consistent with previous studies. A real-world prospective observational study across Europe (Frame study) reported that the OS of patients who received first-line therapy using a platinum-based combination with pemetrexed, gemcitabine, vinorelbine, and taxanes were 10.7, 10.0, 9.1, and 10.7 months, respectively, and there were no significant differences in OS between the groups (all p>0.05) (Moro-Sibilot et al., 2015). Furthermore, a randomized, phase III multicenter trial in patients with advanced or metastatic NSCLC patients reported a similar median OS of 7.9 months for CG, 8.5 months for gemcitabine and paclitaxel, and 8.7 months for PC (Treat et al., 2010).

Toxicity profile is another aspect of chemotherapy regimens. The present study revealed that the incidence of adverse events was greater in the CG group for most chemotherapy-related adverse events (in both hematologic and non-hematologic), except for sensory neuropathy, which was higher in the PC group. This result supported the previous randomized multicenter phase III trial, which reported that patients who were treated with PC had more significant proportions of neurotoxicity and alopecia, while patients who were treated with CG had a higher incidence of myelosuppression (Treat et al., 2010). Although the incidence of chemotherapy-

related adverse events differed significantly between the two groups, this did not significantly affect OS. This is consistent with a recent retrospective study from a resource-limited region of Thailand (Neesanun, 2022), which demonstrated that chemotherapy-related adverse events (e.g., severe neutropenia) were not associated with treatment and survival outcomes, including the response rate, progression-free survival, and OS.

Even though the CG regimen provided a higher rate of chemotherapy-related adverse events, patients in this group tended to achieve more complete cycles of chemotherapy than those in the PC group. This could be because most CG regimen-related adverse events are well tolerated and correctable.

Our study evaluated predictive factors for premature discontinuation of chemotherapy after palliative chemotherapy with platinum-based doublet regimens. There are a few possible reasons explaining why the female sex is a risk factor for achieving complete cycles of chemotherapy. First, women usually develop lung cancer at a younger age than men (Radzikowska et al., 2002), which may significantly affect the tolerability of chemotherapy. Second, the regional cultural background of Asian countries, especially Thailand, teaches women to endure hardships, wherein one study reported that Asian women expressed less emotional distress and experienced less physical difficulties (e.g., pain, side effects of treatment), which may contribute to a favorable quality of life and an increased tolerance to the side effects of chemotherapy (Lim et al., 2009).

Theoretically, poor performance status is found mainly in terminal-stage lung cancer patients and is generally recognized as an unfavorable prognostic factor for OS. A retrospective study in Tunisia reported a mean OS of eight months, and multivariate analysis showed that a performance status ≥2 was a poor prognostic factor (Joobeur et al., 2020). Su et al. reported that performance status (HR=2.487; 95% CI:1.119-5.526; P=0.025) and disease stage (HR=4.015; 95% CI:1.831-8.806; P=0.001) were independent prognostic factors in older patients (≥65 years) with advanced NSCLC in China (Su et al., 2014). Our data indicated that performance status is an important factor in determining survival outcomes in patients with NSCLC. Many factors, including late stage lung cancer, advanced age, high tumor burden, and comorbidities, have a strong relationship with poor performance status, which may influence a low survival rate (Kawaguchi et al., 2010). According to a previous study, treatment with chemotherapy was also related to OS; therefore, we believe that incomplete chemotherapy and partial treatment might impact poor survival outcomes. How et al. (2015) reported a study from a resource-limited country with a median OS of 18 weeks, the independent predictors of death in this study were "no definitive treatment" (HR=2.1; 95%CI,1.4-3.0) and poor performance status (ECOG 3–4) (HR=1.6; 95% CI,1.1-2.3). Multivariate analysis from an observational cohort study showed that factors associated with a reduced likelihood of death included receipt of chemotherapy (HR=0.64) and female sex (HR=0.71) (Salloum et al., 2012). Another study conducted by Yue-Hua Zhang et al. reported that age ≥65 years (HR=1.23, 95% CI, 1.00–1.52), TNM stage (III, HR=1.62, 95% CI, 1.06–2.45; IV, HR=2.31, 95% CI, 1.45–3.68), lung lobectomy (HR=1.93, 95%CI, 1.42–2.63), chemotherapy (HR=1.41, 95% CI, 1.13–1.76), and low pretreatment hemoglobin level (HR=1.54, 95% CI, 1.22–1.94) were independently significantly associated with decreased OS (Zhang et al., 2020).

Our study had several limitations. First, this was a retrospective cohort study that collected data from medical records, which may have led to missing and incomplete data. Second, there were no data on second-line treatment and maintenance therapy, which may influence patient survival. Third, our study did not evaluate cost-effectiveness and quality of life, which may impact the choice of appropriate chemotherapy regimens. Fourth, this study was conducted in a developing country (Thailand), which may have affected the capacity to pay of the patients due to the role of universal health coverage. Fifth, due to the nature of Thai culture, patients and their families may believe that end-stage cancer does not have curable treatment, so they may choose palliative treatment or traditional oriental medicine over chemotherapy (Chang et al., 2018). Finally, at our center, paclitaxel is administered in the conventional free form rather than a nanoparticle formulation, which is more effective and less toxic (Tabrizi et al., 2017). Future trials are needed to evaluate the impact of nanoparticle formulations on survival outcomes.

In conclusion, this study showed that patients treated with CG and PC regimens had no statistically significant difference in OS. The results indicated that both regimens had similar efficacy but had some differences in adverse events. The patients in the CG group tended to have a complete cycle of chemotherapy more than those in the PC group, due to a lower incidence of unacceptable adverse events. First-line chemotherapy should be based on the toxicity profile and patient preference.

Author contribution statement

Conceptualization and design: TB, AC; Methodology: TB, AC; Resources: TB, SU, NN, TR, PK; Writing - original draft: TB, AC; Writing - review and editing: TB, NN, AC; Supervision: AC; Approval of the final version to be published: all authors.

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None.

Ethics approval statement and consent to participate

The protocol was approved by the Institutional Review Board of Hatyai Hospital and carried out according to the Declaration of Helsinki. The requirement of written informed consent was waived since patient information was deidentified before the analysis.

Conflict of interest and source of funding

Thitaya Boonsong, Sirikade Usaha, Narongwit Nakwan, Thidarat Ruklerd, Phungern Khongthong, and Arunchai Chang declare that they have no conflicts of

interest or financial ties to disclose.

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