A Phase II Study of Docetaxel and Carboplatin in Thai Patients with Advanced Non-Small-Cell Lung Cancer

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Objective: *This phase II study aimed to assess the effectiveness of the docetaxel plus carboplatin combination in chemotherapy-na ve Thai patients with advanced non-small-cell lung cancer (NSCLC).*
Material and Method: *Forty patients with Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-1, stage IIIB/IV NSCLC were enrolled in a phase II study between August 2001 and April 2003. Docetaxel 75 mg/m2 and Carboplatin AUC = 6 were given every 3 weeks. Response to treatment and toxicity were graded using standard WHO criteria. The Thai Functional Living Index Cancer (T-FLIC) scale was used to assess the Quality of Life (QoL) of all treated patients.*
Results: *Forty patients (median age: 55 years, range, 39-68 years; PS:0-1) were enrolled: one had stage IIIB disease with effusion, while thirty-nine had stage IV disease. Five patients were non-evaluable due to death within the first cycle; two dying of febrile neutropenia and sepsis, two of pulmonary infection, and one of unknown etiology. Partial response (PR) was seen in 28.6% patients, stable disease (SD) in 25.7%, and progressive disease (PD) in 45.7%. The median survival time was 32 weeks and the 1-year survival rate was 30.7%. Body mass index (BMI) was the only factor associated with survival time (univariate analysis: p = 0.006; multivariate analysis: p = 0.004). Other factors (gender, age, histology, ECOG PS, and glomerular filtration rate) were not predict for survival. The major treatment-related toxicities were neutropenia (from 152 treatment cycles there were grade 4: 19.7%; grade 3: 23.7%), febrile neutropenia (from 152 treatment cycles there was 3.95%), and diarrhea (grades 3/4: 0.66%). The QoL scores improved significantly throughout the treatment period.*
Conclusion: *The regimen of docetaxel and carboplatin is active in advanced NSCLC and may be considered for first-line therapy.*

Keywords: *Docetaxel, Carboplatin, Quality of life, Non-small cell lung cancer*

J Med Assoc Thai 2006; 89 (2): 152-9
Full text. e-Journal: *http://www.medassocthai.org/journal*

Several novel cytotoxic drugs, such as docetaxel, paclitaxel, vinorelbine, gemcitabine, and irinotecan, have been proven to be effective as single agents in the treatment of advanced NSCLC[1]. This has led to the evaluation of combination chemotherapy regimens comprising a platinum compound and a newer cytotoxic agent in an attempt to increase survival, reduce toxicity, increase patient convenience, and improve quality of life (QoL)[2]. A meta-analysis of trials, most of which were conducted prior to the 1990s, has shown a significant survival advantage and improvement of QoL of cisplatin-containing chemotherapy regimens over best supportive care[3-5]. The combination of cisplatin with several new chemotherapeutics agents, including taxanes and vinca alkaloids, has shown superiority over cisplatin-etoposide, cisplatin-teniposide, and other, older cisplatin combinations[5-7]. Furthermore, docetaxel alone and in combination has shown activity against previously untreated advanced NSCLC in several phase II clinical trials[8-11]. Carboplatin has

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shown broad equivalence to cisplatin in combination chemotherapy for advanced NSCLC[12-14]. In phase II trial, the combination of docetaxel and carboplatin was well tolerated, inducing a response rate of 30%, median overall survival of 13.1 months, and 1-year survival rate of 56%[13]. The TAX 326 study examined the effects of two docetaxel plus platinum regimens (cisplatin-docetaxel or carboplatin-docetaxel) against a standard reference regimen of cisplatin-vinorelbine[15]. The present study showed the significant improvement in quality of life. Several investigators[2-4] have reported the benefit of quality of life in advanced NSCLC treated with chemotherapy including the combination of docetaxel plus carbopatin[13]. The impact of chemotherapy on the quality of life was an important aspect of this disease. Functional living Index-Cancer (T-FLIC) which was translated from the original FLIC developed by Harvy Schipper et al[16] and modified by the authors' group and the reliability and validity was reported[17] prior to the usage of this questionnaires to test the quality of life in advanced NSCLC[4]. After that T-FLIC was modified again to version 2 and the test on reliability and validity was confirmed. QoL were evaluated prior to each cycle of chemotherapy using the Thai Functional Living Index Cancer (T-FLIC) scale. The original version of T-FLIC consisted of 22 questions, each with a potential score of 0, 1, or 2. The highest total score was 44. Like the first version, version 2, consisted of 22 questions, but each question now had a potential score of 0, 1, 2, or 3, where a higher score is indicative of a better patient outcome. The highest total score was 66. In this phase II study the primary endpoints were response rate, toxicity, and QoL, the secondary endpoint was survival time.

Material and Method

Eligibility

Eligibility criteria for the present study included pathologically proven NSCLC, stage IIIB/IV disease, age ≥ 18 and < 75 years, ECOG performance status (PS) 0-1, and at least one bidimensionally measurable site of disease. No prior systemic chemotherapy or radiation therapy was permitted for patients with stage IIIB disease. Patients were required to have prestudy hemoglobin ≥ 10 g/dL, absolute neutrophil count ≥ 2 x 109/L, platelets ≥ 100 x 109/L, bilirubin ≤ 1.25 times the upper limit of normal, aspartate aminotransferase ≤ 2 times the upper limit of normal, and creatinine ≤ 1.5 mg/dL. Patients with proven brain or leptomeningeal involvement were excluded, as were those with ≥ grade 1 symptomatic peripheral neuropathy, pregnant or lactating women, and patients with coincident serious medical conditions, including unstable cardiac disease and active uncontrolled infection. Patients were not permitted to receive concomitant treatment with corticosteroids except as prophylaxis for docetaxel-related fluid retention or prophylactic antiemesis. Written informed consent was obtained from all patients, and the protocol was reviewed and approved by the Human Ethics Committee of Faculty of Medicine, Chiang Mai University.

Study treatment

The patients received docetaxel 75 mg/m2 as a 1-hour intravenous (IV) infusion, immediately followed by a carboplatin dose calculated to give an area under the curve carboplatin AUC = 6 according to the Calvert formula[18]. The Cockroft-Gault formula was used to calculate creatinine clearance and determine the carboplatin dose. The docetaxel and carboplatin doses were determined on the basis of a phase I study conducted by Belani et al[19], in which the recommended phase II dose was carboplatin AUC = 6 plus docetaxel 80 mg/m2. In this trial, the docetaxel dose was reduced slightly to 75 mg/m2 to allow easier calculation. All patients received dexamethasone 8 mg twice daily for 4 days, commencing the day prior to chemotherapy. Cycles of chemotherapy were repeated every 3 weeks. Treatment was discontinued if progressive disease (PD) occurred. Patients with stable disease (SD) ceased treatment after 4 cycles. A maximum of 6 cycles of chemotherapy were given to responding patients.

Dose reductions were defined in advance for hematological and nonhematological toxicities. Prophylactic use of granulocyte colony-stimulating factor (G-CSF) was not permitted. The dose of both drugs was reduced by 20% for febrile neutropenia, grade 4 neutropenia of ≥ 7 days duration,or grade 4 thrombocytopenia. Following the first cycle, subsequent cycles were delayed if the pretreatment neutrophil count was < 1.5 x 109/L or if the platelet count was < 100 x 109/L. For grade 2 peripheral neuropathy, the dose of both drugs was reduced by 20%. Patients with grade 3 peripheral neuropathy were taken off the study. Other grade 3 nonhematological toxicities were managed by withholding treatment until resolution to < grade 1 and then restarting treatment with a 20% dose reduction of both drugs. While on the study, patients underwent physical examination and PS testing prior to each cycle of treatment. Computed tomography (CT) scanning or other imaging procedures required to assess disease extent were performed prior

to study treatment and at cycle 4. After completion of study treatment, responder patients were subjected to follow-up by CT scanning at 3 weeks to confirm response. World Health Organization (WHO) criteria were applied to grade response to treatment. The development of brain metastases was considered to indicate PD, even if response outside the brain was demonstrated. Toxicity of chemotherapy was assessed throughout the treatment period. Complete blood counts (CBC) were performed weekly and biochemistry and liver function tests every 3 weeks. Toxicity resulting from treatment was graded according to National Cancer Institute common toxicity criteria (NCI-CTC).

Statistical analysis

Time to disease progression (TTP) and time to death were defined as the time from entry date to disease progression and to death, respectively. The Kaplan-Meier survival curve was used to demonstrate survival patterns over the study period. Cox's proportional hazard model was used to evaluate the effect of one predictor on survival time while controlling for the other predictors. The QoL was assessed at the beginning of each of the 6 chemotherapy cycles. Since at cycle 1, QoL was measured before patients received chemotherapy, this was considered to be the baseline QoL (time 0). The QoL data obtained at the remaining cycles (i.e. cycles 2, 3, 4, 5, and 6) were then designated the time variables 1, 2, 3, 4, and 5, respectively. To assess the change in the QoL score during the treatment period, SAS Proc Mixed Model was applied as it allowed for missing data. For the fixed effects component, a model that used time as a class variable was compared with a simplified model that used time as a quantitative variable. The significance of baseline QoL scores as predictors of subsequent QoL scores was also evaluated. Each patient was considered to constitute a random effect. Different covariance structures between repeated QoL measurements were also modeled and compared. The appropriateness of Mixed Model assumptions was assessed using residuals analysis. Mixed Models were fitted separately for the total QoL score, physical wellbeing score, and psychological wellbeing score. All statistical data analyses were performed using SAS Version 8.1.

Results

Patient characteristics

A total of 40 patients were enrolled in this trial between August 2001 and April 2003. Five patients were considered nonevaluable: two had pulmonary infection and died within the first cycle without neutropenia; one died of unknown etiology; another two had febrile neutropenia and died during the first cycle. The characteristics of the 40 patients enrolled are shown in Table 1.

Table 1. Patient characteristics (n = 40)

Median Age (Range)	55 (39; 68) yrs
Sex:	
Female	14 (35.0%)
Male	26 (65.0%)
ECOG PS:	
1	21 (52.5%)
0	19 (47.5%)
BMI*	
< 20	20 (50.0%)
≥ 20	20 (50.0%)
Histology:	
Squamous	15 (37.5%)
Adenocarcinoma	21 (52.5%)
Large cell	3 (7.5%)
Undifferentiated	1 (2.5%)
GFR**	
< 60	21 (52.5%)
≥ 60	19 (47.5%)
Stage:	
IIIb	1 (2.5%)
IV	39 (97.5%)
Site of metastasis:	
Lung only	18 (45.0 %)
Bone only	3 (7.5 %)
≥ 2 sites	19 (47.5%)

* BMI = Body Mass Index
* * GFR = glomerular filtration rate

Table 2. Response to the treatment (n = 35)

Complete response (CR)	0	
Partial response (PR)	10	(28.6%)
Stable disease (SD)	9	(25.7%)
Progressive disease (PD)	16	(45.7%)
Median disease progression (TTP) (range: weeks)	15.7*	(2.9-64.4)
Median survival time (range: weeks)	30*	(1-140^{+})

* Kaplan-Meier's estimate

Table 3. Results of univariate and multivariate analyses

			KM Median*	Log-rank	Cox's Regression		
	n	Dead (%)	Survival time (days)	*p*-value	Crude HR** (95%CI)	Adjusted HR** (95%CI)	*p*-value
Sex:							
Female	14	11 (78.6%)	31.9	0.626	1	1	0.948
Male	26	22 (84.6%)	35.3		1.20 (0.57, 2.52)	0.97 (0.42, 2.23)	
Age (yrs):							
< 65	35	28 (80%)	34.6	0.279	1	1	0.291
≥ 65	5	5 (100%)	5.7		1.69 (0.64, 4.46)	1.82 (0.60, 5.51)	
BMI:							
< 20	20	20 (100%)	26.3	0.006	2.70 (1.30, 5.59)	3.50 (1.49, 8.21)	0.004
≥ 20	20	13 (65%)	50.0		1	1	
Histology:							
Squamous	15	13 (86.7%)	35.3	0.671	1.17 (0.57, 2.37)	0.94 (0.43, 2.06)	0.872
Other	25	20 (80.0%)	33.9		1	1	
Karnofsky PS:							
< 80	21	17 (80.9%)	35.3	0.722	1	1	0.347
≥ 80	19	16 (84.2%)	31.9		1.13 (0.57, 2.25)	1.45 (0.67, 3.17)	
GFR***:							
< 60	21	18 (85.7%)	35.3	0.956	1	1	0.265
≥ 60	19	15 (78.9%)	26.3		1.02 (0.51, 2.04)	1.60 (0.70, 3.65)	

* Kaplan-Meier's estimate
** HR = hazard ratio
*** GFR = glomerular filtration rate

There were 26 males and 14 females.The median age of the patients was 55 years (range, 39-68 years). Twenty-one cases had ECOG performance status (PS) 1, and nineteen cases had PS 0. Twenty-one cases were adenocarcinoma and 97.5% were stage IV. Nineteen cases had two or more metastatic sites.

Response

Of the 35 patients evaluable for response, none exhibited complete response (CR). Partial response (PR) was seen in 28.6%, SD in 25.7%, and PD in 45.7% (Table 2). The median survival time was 32 weeks and the 1-year survival rate was 30.7%.(Fig 1). Body mass index (BMI) was the only factor associated with survival time (Table 3).

Quality of Life (QoL)

Of the 40 patients, the QoL of 7 patients was measured only once at baseline (time 0), and of a further 6 patients at baseline (time 0) and at time 1. Since QoL at baseline was used as a predictor for the subsequent QoL, the 7 patients whose QoL was

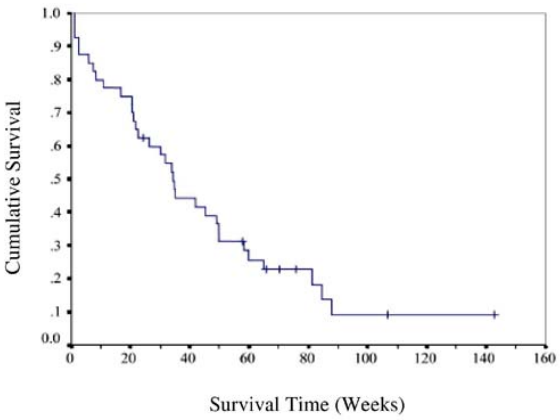

Fig. 1 Kaplan-Meier estimate of overall survival

measured only at baseline were excluded from the Mixed Model analysis. Also, to establish a reasonable covariance structure between repeated QoL measurements over 5 cycles, only those patients whose QoL was measured at least at times 1 and 2 were included. A total of 27 subjects were, therefore, included in the Mixed Model analysis. Based on all 40 patients enrolled in the study, simple descriptive statistics revealed that the QoL of patients seemed to improve as time passed (Table 4). Results from the present study obtained from Mixed Models showed that baseline QoL scores were statistically significant predictors of subsequent QoL scores. The Mixed Model that used time (1, 2, 3, 4, 5) as a class variable was significantly better than the model that used time as a quantitative variable. Therefore, significant fixed effects in the Mixed Model were baseline QoL (time 0) and time (1, 2, 3, 4, 5) used as a class variable. For the covariance structure of the QoL repeated over time, it was found that auto regressive (AR) order 1 was adequate and that the correlation between two repeated QoL measures decreased over time. If the correlation coefficient between QoL measured at times 1 and 2 is r, then the correlation between times 1 and 3 is r2, between times 1 and 4 r3, and between times 1 and 5 r4, respectively. Table 4 displays the results obtained from the Mixed Model fitting of total QoL scores, the physical wellbeing score, and the psychological wellbeing score. Predicted Least Squares (LS) means of QoL scores obtained at each time (1, 2, 3, 4, 5) were calculated using baseline (time 0) QoL scores and are displayed in Table 5. For a total QoL score at baseline of 44.50, the predicted scores at times 1, 2, 3, 4, and 5 are 46.17, 49.28, 49.26, 49.27, and 50.11, respectively. The differences in total QoL scores at time 1 vs times 2, 3, 4, and 5 were significant, whereas the other paired differences were not (data not shown). This pattern was also replicated in the physical wellbeing score and the psychological wellbeing score.

Toxicity

A total of 152 cycles of treatment were given, the median number received being 4 (range, 1-6 cycles). Twelve patients (34.28%) received 6 cycles. Neutropenia was the predominant hematological toxicity. Grades 3/4 neutropenia occurred in 23.68% and 19.74% of treatment cycles, respectively. There were six episodes of febrile neutropenia, while thrombocytopenia was rare. Grades 2/3 anemia was seen in 25% and 7.89% of patients, respectively. Besides febrile neutropenia and sepsis, pneumonia and respiratory failure were the main causes of death during the first cycle of treatment. Mild episodes of nausea, vomiting, diarrhea, and fatigue were observed.

Table 4. Descriptive statistics of observed QoL at each cycle

	Cycle	Patients (n)	Mean	SD	Min, Max
Total QoL (0-66)	0	40	44.5	8.5	20, 58
	1	33	45.7	9.9	22, 64
	2	27	50.4	8.5	34, 64
	3	26	50.9	8.3	34, 65
	4	14	54.1	6.4	43, 63
	5	12	54.4	6.3	43, 64
Physical Wellbeing (0-27)	0	40	17.3	3.6	7, 22
	1	33	17.9	4.4	7, 25
	2	27	20.1	4.1	12, 26
	3	26	20.2	3.9	12, 26
	4	14	22.0	2.9	18, 26
	5	12	22.1	2.7	18, 26
Psychological Wellbeing (0-18)	0	40	13.4	2.6	6, 18
	1	33	14.3	2.4	9, 18
	2	27	15.1	2.3	11, 18
	3	26	15.3	2.3	12, 18
	4	14	16.0	1.9	13, 18
	5	12	15.9	1.9	13, 18

Table 5. Predicted least squares (LS) QoL mean scores at time 1, 2, 3, 4, 5 (Time 0 scores = Actually measured)

	Time	LS Means	Significant Pairwise Differences		
			Time	Difference	*p*-value
Total QoL score (0-66)	0	44.50*			
	1	46.17	1 vs 2	3.11	<0.0001
	2	49.28	1 vs 3	3.09	0.0022
	3	49.26	1 vs 4	3.10	0.0202
	4	49.27	1 vs 5	3.94	0.0131
	5	50.11			
Physical Wellbeing QoL Score (0-27)	0	17.30*			
	1	18.32	1 vs 2	1.52	0.0016
	2	19.84	1 vs 3	1.40	0.0258
	3	19.72	1 vs 4	1.79	0.0312
	4	20.11	1 vs 5	2.24	0.0206
	5	20.56			
Psychological Wellbeing QoL Score (0-18)	0	13.40*			
	1	14.32	1 vs 2	0.52	0.0021
	2	14.84	1 vs 3	0.55	0.0156
	3	14.87	1 vs 4	0.76	0.0134
	4	15.08	1 vs 5	0.85	0.0207
	5	15.17			

*Observed baseline QoL score

Discussion

This phase II study evaluated the combination of docetaxel and carboplatin in Thai patients with advanced NSCLC. The overall response rates (CR + PR) was 28.57%, a 1-year survival rate of 30.7%, and a median survival of 32 weeks (range, 1-140+ weeks). These results are consistent with others obtained using this two-drug combination. The response rate of docetaxel plus carboplatin reported in TAX 326 study[15] was similar to the authors' finding (response rate of 32.9%, median survival of 9.4 months and one year survival was 18%.

Millward et al[20] reported the result of phase II study using the same combination in stage III and IV NSCLC and had a response rate of 39% and a 1-year survival rate of 53%. The only significant predictor of response in that study was ethnicity (Asian versus Caucasian).

The present study was conducted in an entirely Asian population. The authors cannot conclude that response rate and toxicities observed are related to ethnicity, since these outcomes did not differ greatly from those reported elsewhere[15,19] A major prognostic parameter in the presented patient population may be low BMI. The reason that the authors used BMI as a prognostic factors because there was no data on weight loss in the presented study population, thus initial BMI may possibly be used instead of weight loss. In the present study hematological toxicity was common. The majority of patients developed grade 4 neutropenia, accompanied by febrile neutropenia in 3.95% of cycles, most cases developing within the first cycle. The use of prophylactic antibiotics or G-CSF was not permitted on this protocol, but could be considered in patients with febrile neutropenia. Diarrhea was the most significant nonhematological toxicity. Renal or electrolyte problems occurred rarely. Since chemotherapy is primarily palliative in advanced NSCLC, the influence on patients' QoL is an important consideration in the evaluation of any new therapy. NSCLC treated with docetaxel plus carboplatin in the present study, confirmed that QoL improved significantly throughout the treatment period, indicating that the combination was well tolerated. These findings are consistent with those of other studies[15]. Thus, the authors conclude that the combination of docetaxel plus carboplatin is active in NSCLC and may be considered as a first-line treatment option.

Acknowledgments

This work was supported by a grant from Aventis Pharmaceuticals, Thailand.

The authors wish to thank Miss Chulaluk Komoltri (Biostatistics), and Miss Kanittha Thaikla for their assistance with the statistical analyses.

References

1. Ramalingam S, Belani CP. State-of-the-art chemotherapy for advanced non-small cell lung cancer. Semin Oncol 2004; 31(Suppl 1): 68-74.
2. Harper P. Management of advanced non small cell lung cancer [abstract]. Proceedings 15th International Congress on Anti-Cancer Treatment (ICACT), Paris, 9-12 Feb 2004: 158-64.
3. Non-small Cell Lung Cancer Collaborative Group. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomised clinical trials. BMJ 1995; 311: 899-909.
4. Thongprasert S, Sanguanmitra P, Juthapan W, Clinch J. Relationship between quality of life and clinical outcomes in advanced non-small cell lung cancer: best supportive care (BSC) versus BSC plus chemotherapy. Lung Cancer 1999; 24: 17-24.
5. Bonomi P, Kim K, Fairclough D, Cella D, Kuler J, Rowinsky E, et al. Comparison of survival and quality of life in advanced non-small-cell lung cancer patients treated with two dose levels of paclitaxel combined with cisplatin versus etoposide with cisplatin: results of an Eastern Cooperative Oncology Group trial. J Clin Oncol 2000; 18: 623-31.
6. Giaccone G, Splinter TA, Debruyne C, Kho GS, Lianes P, van Zandwijk N, et al. Randomised study of paclitaxel-cisplatin versus cisplatin-teniposide in patients with advanced non-small-cell lung cancer. The European Organization for Research and Treatment of Cancer Lung Cancer Cooperative Group. J Clin Oncol 1998; 16: 2133-41.
7. Le Chevalier T, Brisgand D, Douillard JY, Pujol JL, Alberola V, Monnier A, et al. Randomised study of vinorelbine and cisplatin versus vindesine and cisplatin versus vinorelbine alone in advanced non-small-cell lung cancer: results of a European multicenter trial including 612 patients. J Clin Oncol 1994; 12: 360-7.
8. Francis PA, Rigas JR, Kris MG, Pisters KM, Orazem JP, Woolley KJ, et al. Phase II trial of docetaxel in patients with stage III and IV non-small-cell lung cancer. J Clin Oncol 1994;12:1232-7.
9. Zalcberg J, Millward M, Bishop J, McKeage M, Zimet A, Toner G, et al. Phase II study of docetaxel and cisplatin in advanced non-small-cell lung cancer. J Clin Oncol 1998; 16: 1948-53.
10. Georgoulias V, Androulakis N, Dimopoulos AM, Kourousis C, Kakolyris S, Papadakis E, et al. First-line treatment of advanced non-small-cell lung cancer with docetaxel and cisplatin: a multicenter phase II study. Ann Oncol 1998; 9: 331-4.
11. Zaragoulidis K, Kontakiotis T, Hatziapostolou P, Fachantidou E, Delis D, Goutsikas J, et al. A phase II study of docetaxel and carboplatin in the treatment of non-small cell lung cancer. Lung Cancer 2001; 32: 281-7.
12. Klastersky J, Sculier JP, Lacroix H, Dabouis G, Bureau G, Libert P, et al. A randomised study comparing cisplatin or carboplatin with etoposide in patients with advanced non-small-cell lung cancer: European Organization for Research and Treatment of Cancer protocol 07861. J Clin Oncol 1990; 8: 1556-62.
13. Jelic S, Mitrovic L, Radosavjelic D, Elezar E, Babovic N, Kovcin V, et al. Survival advantage for carboplatin substituting cisplatin in combination with vindesine and mitomycin C in patients with stage IIIB and IV squamous-cell bronchogenic carcinoma: a randomised phase III study. Lung Cancer 2001; 34: 1-13.
14. Gatzemeier U, Rosell R, Betticher D, Keppler U, Macha HN, Pirker R, et al. Randomised pan-European trial comparing paclitaxel (TAX)/carboplatin (CAR) versus paclitaxel/cisplatin (CIS) in advanced non-small-cell lung cancer (NSCLC). Eur J Cancer 1999; 35(Suppl 4): 246.
15. Fossella F, Pereira JR, von Pawel J, Pluzanska A, Gorbounova V, Kaukel E, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: the TAX 326 study group. J Clin Oncol 2003; 21: 3016-24.
16. Schipper H, Levitt M. Measuring quality of life: risks and benefits. Cancer Treat Rep 1985; 69: 1115-23.
17. Sanguanmitra P, Juthapan W, Thongprasert S. Validity and reliability of the modified Functional Living Index-Cancer (T-FLIC) and the modified quality of life (T-QLI) questionnaires. In: Proceedings of the 11th Asia Pacific Cancer Conference, Bangkok, Thailand. 1993: 121.
18. Calvert AH, Newell DR, Gumbrell LA, O'Reilly S, Burnell M, Boxall FE, et al. Carboplatin dosage:

prospective evaluation of a simple formula based on renal function. J Clin Oncol 1989; 7: 1748-56.
19. Belani CP, Einzig A, Bonomi P, Dobbs T, Capozzoli MJ, Earhart R, et al. Multicenter phase II trial of docetaxel and carboplatin in patients with stage IIIB and IV non-small-cell lung cancer. Ann Oncol 2000; 11: 673-8.
20. Millward MJ, Boyer MJ, Lehnert M, Clarke S, Rischin D, Goh BC, et al. Docetaxel and carboplatin is an active regimen in advanced non-small-cell lung cancer: a phase II study in Caucasian and Asian patients. Ann Oncol 2003; 14: 449-54.

การศึกษา Phase II เพื่อประเมินประสิทธิภาพของยาเคมีบำบัด Docetaxel ร่วมกับ Carboplatin ในผู้ป่วยมะเร็งปอดชนิด Non-small cell

สุมิตรา ทองประเสริฐ, สิริกุล ศรฤทธิ์ชิงชัย, บุษยามาส ชีวสกุลยง, ชัยยุทธ เจริญธรรม, สุทธิรักษ์ มูลประการ

ผู้ป่วย 40 รายเป็นมะเร็งปอดชนิด Non-small cell ระยะ IIIB-IV ซึ่งมีสุขภาพอยู่ในเกณฑ์ 0-1 (ประเมินโดย ECOG) เข้ารับการรักษาในช่วงสิงหาคม พ.ศ. 2544 ถึง เมษายน พ.ศ. 2546 ผู้ป่วยได้รับยา Docetaxel ขนาด 75 มิลลิกรัมต่อตารางเมตร และ Carboplatin ขนาด AUC เท่ากับ 6 โดยซ้ำทุก 3 สัปดาห์ ประเมินการตอบสนองโดยใช้เกณฑ์ของ WHO และประเมินคุณภาพชีวิตโดยใช้ T-FLIC version 2

ผลการศึกษาพบว่า ผู้ป่วย 40 ราย มีอายุเฉลี่ย 55 ปี (39-68 ปี) ค่า PS เท่ากับ 0-1 ผู้ป่วย 1 รายเป็นมะเร็งในระยะ IIIB ซึ่งมีน้ำในช่องปอดร่วมด้วย ผู้ป่วย 39 รายเป็นมะเร็งระยะ IV ผู้ป่วย 5 รายถึงแก่กรรมในระหว่างรับยาชุดที่ 1 โดย 2 รายเสียชีวิตจากการติดเชื้อ ขณะเม็ดเลือดขาวต่ำ ผู้ป่วยอีก 2 รายเสียชีวิตจากการติดเชื้อในปอด และ 1 รายเสียชีวิตที่บ้านโดยไม่ทราบสาเหตุ

พบการตอบสนองแบบไม่สมบูรณ์ ร้อยละ 28.6 ตอบสนองแบบคงที่ ร้อยละ 25.7 และโรคกำเริบ ร้อยละ 45.7 ค่าเฉลี่ยของการรอดชีวิต 32 สัปดาห์ และอัตรา การรอดชีวิตที่ 1 ปี ร้อยละ 30.7 จากการศึกษาปัจจัยสำหรับการพยากรณ์โรค พบ Body Mass Index เป็นปัจจัยเดียวที่สัมพันธ์กับการรอดชีวิต ผลข้างเคียงที่สำคัญคือเม็ดเลือดขาวต่ำ พบเกรด 4 ร้อยละ 19.7 เกรด 3 ร้อยละ 23.7 ค่าคุณภาพชีวิตเพิ่มตลอดการรักษา

***สรุป**: ยา Docetaxel และ Carboplatin เป็นยาที่มีประสิทธิภาพในการรักษามะเร็งปอด Non-small cell และควรพิจารณานำมาใช้เป็น First-line treatment*