

# Quality of Life in Advanced Non-Small Cell Lung Cancer Receiving Chemotherapy of Platinum Combination in Old versus New Standard Chemotherapy Regimen

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**Background and Objective:** Non-small cell lung cancers (NSCLC) mostly are adenocarcinoma but minor squamous cell carcinoma is related to smoking. Surgery has a major role in early stage with chemotherapy or radiation in advanced stage. Platinum combination chemotherapy could increase the progression free survival which may be combined with etoposide as the old standard regimen or paclitaxel/gemcitabine as the new standard regimen with slightly more benefit. This study was conducted to evaluate quality of life (QoL) and response of chemotherapy.

**Material and Method:** The prospective study in advanced NSCLC enrolled 88 patients receiving chemotherapy with old or new standard regimen in the Oncology Unit, Medicine Department of Rajavithi Hospital from January 2004 to December 2009. The assessments were composed of the result of treatment and QoL evaluated by Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L) in both groups.

**Results:** The 88 advanced NSCLC patients received old standard chemotherapy 49 cases and new standard chemotherapy 39 cases. No statistically significant difference was found in baseline characteristics and most had adenocarcinoma subtype. The overall QoL scores before and after treatment were similar except a slight decrease in social/family well-being. The overall response rate was increased in the new standard regimen group compared with the old regimen group (61.5% versus 24.5%) but without statistical difference in median progression free survival (23 and 20 weeks, respectively).

**Conclusion:** New standard chemotherapy regimen demonstrated increased overall response rate and without decreased QoL.

**Keywords:** Advanced non-small cell lung cancer, Platinum combination chemotherapy, Functional assessment of cancer therapy-lung cancer (FACT-L), Quality of life

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The incidence of lung cancer in Thailand is 15.0% in all cancer types and slightly more in males and in the northern region but with a high death rate 25.0-30.0%<sup>(1)</sup>. This cancer can be classified in two types: non-small cell lung cancer (NSCLC) 84.0%<sup>(2)</sup> and small cell lung cancer (SCLC) 16%. Squamous cell lung cancer, subtype NSCLC and SCLC are related to smoking behavior<sup>(3-5)</sup>.

Chemotherapy is mostly used in advanced stage IIIb-IV reported by American Joint Committee on Cancer (AJCC) classification to improve progression

free survival and improved quality of life (QoL). Among patients with the eastern cooperative oncology group (ECOG) performance status was reported as less than 2 compared with the best supportive treatment<sup>(6-8)</sup>. Platinum base combination chemotherapy 4-6 cycles has demonstrated more benefit than single agent treatment<sup>(9-13)</sup>. The platinum combination regimens were classified in the old standard regimen, e.g., cisplatin or carboplatin combined with etoposide, which has been often used in the past. In addition, the new standard regimen, e.g., cisplatin or carboplatin combined with paclitaxel or gemcitabine has been reported to have more beneficial response and convenience to use in the out-patient unit<sup>(14-16)</sup>.

The result of treatment and QoL assessment are gold standard evaluations in cancer therapy. QoL is classified in four main domains: health and

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functioning, psychological and spiritual, social and economic and family well-being<sup>(17-25)</sup>. The functional assessment of cancer therapy-lung cancer (FACT-L) is a tool to assess QoL of lung cancer patients commonly used in the United States, adapted from version 4 and translated in many languages in Asia including Thai<sup>(26-30)</sup>. The objective of this study was to compare QoL and evaluate the result of old versus new standard chemotherapy regimens of advanced NSCLC.

### Material and Method

A prospective cohort study was conducted by examining medical profiles of patients diagnosed with NSCLC stage IIIb-IV, in the Oncology Unit, Department of Medicine, Rajavithi Hospital from January 2004 to December 2009. They received chemotherapy regimen according to their reimbursement status and analyzed in two types of chemotherapy: old standard regimen in the social well fair patients (carboplatin/etoposide) and new standard regimen in the government reimbursement patients (carboplatin/paclitaxel as the major component, more than 90% and carboplatin/gemcitabine as the minor). These patients were at their first diagnosis of cancer with no previous chemotherapy treatment, had ECOG performance status 0-1, including normal complete blood count, liver and renal function. Their QoL was evaluated by FACT-L questionnaire at three periods: first; before starting chemotherapy treatment, second; during treatment 2-4 cycles and third; after treatment at 5-6 cycles. Their negative questionnaire scores were converted in the data collecting process with a high score meaning good QoL. The result of treatment was evaluated using RECIST criteria<sup>(31)</sup>.

The present study was approved by the Research and Ethics Committee of Rajavithi Hospital.

### Statistical analysis

The result from the previous study of Belani<sup>(16)</sup> reported the response of new chemotherapy increased more than 30% and unchanged QoL after receiving chemotherapy and the difference between old and new chemotherapy was estimated at less than 30%. The authors needed to collect at least 74 patients for both groups to detect significant differences in chemotherapy and QoL from 50% to 80% with 70% power and alpha-level 0.05.

Baseline characteristics of categorical data between the two groups were calculated by Pearson Chi-square or Fisher's exact test and Independent Sample t-test for the continuous data between the two

groups. The comparison of QoL before and after treatment within group was calculated by Paired t-test and Independent Sample t-test between the two groups. The progression free survival was estimated using the Kaplan-Meier method and comparison was made between groups by the Log-rank test.

The progression free survival calculation was started from the date of diagnosis until date of disease progression or death as a result of any cause. Statistical analysis was performed with SPSS version 17.0.

### Results

The 88 patients were divided between old standard regimen group comprising 49 cases and new standard regimen group comprising 39 cases as shown in Table 1. The clinical characteristics were not significantly different between both groups. Most were married, males, more than 50 years old, smoking less than one year or nonsmoking, had weight loss less than 10%, no co-morbidity and adenocarcinoma cell subtype.

Table 2 and Table 2.1 shows QoL scores before treatment of the new regimen group demonstrated slightly higher overall scores for emotional, functional well-being, and additional concerns, with significant difference. After follow-up, during and after treatment at the second and third QoL assessment, no significant difference was observed in overall well-being in both groups but tended to decreased for social/family well-being.

The overall response result including partial response and stable disease was significantly increased in the new regimen treatment group compared with the old regimen (61.5% and 24.5%, respectively) but with no observable difference in median progression free survival.

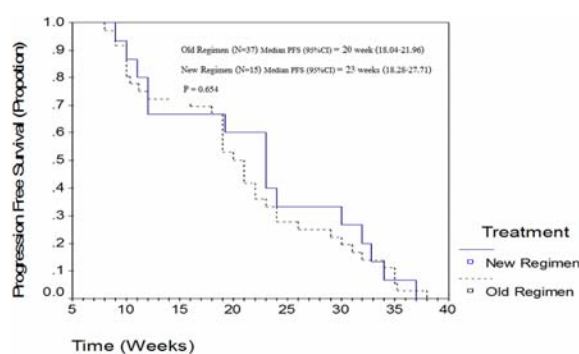


Fig. 1 Kaplan-Meier estimates of progression free survival.

**Table 1.** Baseline characteristics of 88 patients

	Old regimen n = 49 n (%)	New regimen n = 39 n (%)	p-value
Age (year) mean $\pm$ SD	54 $\pm$ 10.75	55.5 $\pm$ 12.81	0.070
Sex			0.274
Male	40 (81.6%)	28 (71.8%)	
Female	9 (18.4%)	11 (28.2%)	
Status			0.544
Married	39 (79.6%)	33 (84.6%)	
Single/divorced	10 (20.4%)	6 (15.4%)	
Comorbid illness			0.603
No	38 (77.6%)	32 (82.1%)	
Yes	11 (22.4%)	7 (17.9%)	
Education			<0.001*
Below bachelor degree	48 (98.0%)	26 (66.7%)	
Bachelor degree	1 (2.0%)	13 (33.3%)	
Debt burden			0.251
No	46 (93.9%)	39 (100%)	
Yes	3 (6.1%)	0 (0.0%)	
Smoking			0.464
No/less than 1 year	35 (71.4%)	25 (64.1%)	
More than 1 year	14 (28.6%)	14 (35.9%)	
Weight loss			0.759
<10%	35 (71.4%)	29 (74.4%)	
>10%	14 (28.6%)	10 (25.6%)	
Cell type			0.269
Adenocarcinoma	36 (73.5%)	34 (87.2%)	
Squamous	6 (12.2%)	3 (7.7%)	
Other/cytology	7 (14.3%)	2 (5.1%)	
Organ metastasis			0.127
Lung/pleura	43 (87.8%)	38 (97.4%)	
Other site(s)	6 (12.2%)	1 (2.6%)	
ECOG performance status			0.127
PS = 0	43 (87.8%)	38 (97.4%)	
PS = 1	6 (12.2%)	1 (2.6%)	

\* Significant at  $p < 0.05$ 

ECOG = the eastern cooperative oncology group

**Discussion**

The reasons to use the new chemotherapy regimen (carboplatin/paclitaxel as the major component, more than 90% and carboplatin/gemcitabine as the minor) more than the old chemotherapy regimen (cisplatin or carboplatin/etoposide) to treat NSCLC are maintenance of QoL and convenience: as one-day compared with three-day treatment. The QoL score was slightly higher in the new regimen group before starting treatment, and this may be related to the higher educational status and greater income in this group. After treatment at the second and third QoL assessment no difference was demonstrated in both groups and overall well-being did not decrease. These may indicate

minimal side effects from the treatment in both groups and the patients could adapt and cope with the disease and treatment. The chemotherapy of the platinum combination in the old and new regimen often used carboplatin more than cisplatin because of fewer side effects, no need to admit for hydration and comparable results as reported in many studies<sup>(30,32-36)</sup>. The result of chemotherapy demonstrated increased overall response in the new regimen treatment, compatible with other studies<sup>(32,33)</sup>. However, the progression free survival in both groups showed no significant difference but tended to slightly increase in the new standard regimen group.

Compared with other studies in Thailand, five

**Table 2.** QoL assessment before, during and after treatment in both groups

QoL	Old regimen Mean $\pm$ SD	New regimen Mean $\pm$ SD	<i>p</i> -value
Before treatment (n)	49	39	
Physical well-being (GP)	3.70 $\pm$ 0.66	3.70 $\pm$ 0.61	0.986
Social/family well-being (GS)	4.52 $\pm$ 0.35	4.61 $\pm$ 0.41	0.249
Emotional well-being (GE)	3.75 $\pm$ 0.76	4.13 $\pm$ 0.80	0.025*
Functional well-being (GF)	2.95 $\pm$ 0.76	3.33 $\pm$ 0.74	0.023*
Additional concerns(C)	3.26 $\pm$ 0.45	3.51 $\pm$ 0.56	0.025*
Overall first assessment	3.61 $\pm$ 0.44	3.87 $\pm$ 0.43	0.007*
During treatment 2-4 cycles (n)	49	39	
Physical well-being (GP)	3.82 $\pm$ 0.65	3.73 $\pm$ 0.65	0.532
Social/family well-being (GS)	4.53 $\pm$ .35	4.58 $\pm$ 0.37	0.522
Emotional well-being (GE)	3.82 $\pm$ 0.76	3.97 $\pm$ 0.77	0.383
Functional well-being (GF)	3.13 $\pm$ 0.73	3.26 $\pm$ 0.68	0.399
Additional concerns (C)	3.42 $\pm$ 0.61	3.38 $\pm$ 0.47	0.732
Overall second assessment	3.71 $\pm$ 0.49	3.76 $\pm$ 0.42	0.614
After treatment 5-6 cycles (n)	42	36	
Physical well-being (GP)	3.59 $\pm$ 0.58	3.79 $\pm$ 0.52	0.125
Social/family well-being (GS)	4.45 $\pm$ 0.50	4.43 $\pm$ 0.48	0.912
Emotional well-being (GE)	3.79 $\pm$ 0.69	3.92 $\pm$ 0.73	0.428
Functional well-being (GF)	3.20 $\pm$ 0.87	3.21 $\pm$ 0.72	0.957
Additional concerns (C)	3.34 $\pm$ 0.64	3.30 $\pm$ 0.50	0.718
Overall third assessment	3.63 $\pm$ 0.50	3.68 $\pm$ 0.42	0.586

\* Significant (2-tailed) t-test, high score mean good QoL

**Table 2.1.** Comparing QoL assessment before and after treatment in both groups

QoL	Old regimen Mean $\pm$ SD n = 49	New regimen Mean $\pm$ SD n = 39	<i>p</i> -value
Physical well-being (GP)	-0.11 $\pm$ 0.72	0.09 $\pm$ 0.72	0.172
Social/family well-being (GS)	-0.07 $\pm$ 0.45	-0.18 $\pm$ 0.60	0.451
Emotional well-being (GE)	0.04 $\pm$ 1.07	-0.21 $\pm$ 1.05	0.480
Functional well-being (GF)	0.25 $\pm$ 1.04	-0.12 $\pm$ 0.96	0.305
Additional concerns (C)	0.08 $\pm$ 0.70	-0.21 $\pm$ 0.56	0.168
Overall assessment	0.02 $\pm$ 0.86	-0.19 $\pm$ 0.54	0.215

**Table 3.** The result of treatment

Result	New regimen (n = 39)	Old regimen (n = 49)	<i>p</i> -value
Overall response rate (%)	24 (61.5%)	12 (24.5%)	0.001*
Partial response (%)	7 (17.9%)	1 (2.0%)	-
Stable disease (%)	17 (43.6%)	11 (22.4%)	-
Progression (%)	15 (38.5%)	37 (75.5%)	0.001*

\*Significance at  $p < 0.05$

years before, our patients demonstrated a lower mean age<sup>(37-39)</sup>. This may refer to greater amounts of impure

agents in the air leading to lung cancer developing at an early age.

## Conclusion

The new chemotherapy regimen demonstrated increased overall response and with no decreased QoL score. Although the old chemotherapy regimen produced a lower response, the treatment was less expensive with similar results for progression free survival and QoL.

## Potential conflicts of interest

None.

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## คุณภาพชีวิตในกลุ่มผู้ป่วยมะเร็งปอดชนิดเซลล์ไม่เล็กกระยะลุกลามที่ได้รับการรักษาด้วยเคมีบำบัดกลุ่มเก่าและกลุ่มใหม่

เจษฎา มณีชวขจร, จิรเจษฎ์ สุขสุเพิ่ม

ภูมิหลังและวัตถุประสงค์: มะเร็งปอดชนิดเซลล์ไม่เล็ก non-small-cell lung cancer (NSCLC) พบได้บ่อยส่วนใหญ่เป็น adenocarcinoma ส่วนน้อยเป็นชนิด squamous cell carcinoma ซึ่งสัมพันธ์กับการสูบบุหรี่หรือการรักษาลูกได้แก่ การผ่าตัดสำหรับผู้ป่วยระยะแรก การฉายรังสีสำหรับรอยโรคที่ผ่าตัดไม่ได้ ระยะลุกลามใช้ยาเคมีบำบัดสูตร platinum combination สามารถเพิ่มการรอดชีวิตและชะลอการกระจายของโรค ยาสูตรใหม่ เช่น platinum และ paclitaxel หรือ gemcitabine มีการตอบสนองดีกว่ายาสูตรเก่าเช่น platinum และ etoposide แต่ก็มีผลแทรกซ้อนที่ต่างกันออกไป ซึ่งอาจส่งผลถึงคุณภาพชีวิตของผู้ป่วย การวิจัยนี้ทำขึ้นเพื่อศึกษาถึงคุณภาพชีวิตที่เปลี่ยนแปลงหลังการรักษา รวมทั้งผลการตอบสนองเปรียบเทียบระหว่างยาแต่ละกลุ่ม

วัตถุประสงค์และวิธีการ: ได้ทำการรวบรวมผู้ป่วย NSCLC ระยะลุกลามจำนวน 88 ราย ที่มารับยาเคมีบำบัด ณ หน่วยงานโรคมะเร็ง กลุ่มงานอายุรศาสตร์ โรงพยาบาลราชวิถี ตั้งแต่ เดือนมกราคม พ.ศ. 2547 ถึง ธันวาคม พ.ศ. 2552 โดยศึกษาถึงข้อมูลพื้นฐานประชากร ประเมินคุณภาพชีวิตด้วยแบบสอบถาม functional assessment of cancer therapy-lung cancer (FACT-L) และประเมินผลการรักษาเปรียบเทียบระหว่างกลุ่มที่ได้รับ platinum combination ของยากลุ่มเก่าที่ประกอบด้วย cisplatin หรือ carboplatin ร่วมกับ etoposide และยากลุ่มใหม่ที่ประกอบด้วย cisplatin หรือ carboplatin ร่วมกับ paclitaxel หรือ gemcitabine

ผลการศึกษา: ผู้ป่วยทั้งหมด 88 ราย เป็นชาย 68 ราย หญิง 20 ราย แบ่งเป็นกลุ่มที่ได้ยาเก่า 49 ราย ยาใหม่ 39 ราย ลักษณะทั่วไปและลักษณะทางคลินิกใกล้เคียงกันเกือบทั้งหมดเป็น adenocarcinoma คุณภาพชีวิตที่เปลี่ยนแปลงก่อนและหลังให้ยาใกล้เคียงกันแต่คุณภาพชีวิตด้านครอบครัวและสังคมมีแนวโน้มที่จะลดลง ผู้ป่วยที่ได้รับยากลุ่มใหม่มีการตอบสนองดีกว่า (61.5% และ 24.5% ตามลำดับ) ส่วน median progression free survival ไม่แตกต่างจากยาเก่า (23 และ 20 สัปดาห์)

สรุป: การรักษาด้วยยาเคมีบำบัดกลุ่มใหม่เมื่ออัตราการตอบสนองดีกว่ายาเก่าไม่ทำให้คุณภาพชีวิตลดลง ดังนั้นสมควรใช้ในการรักษา advanced NSCLC

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