

# Prognostic Factors for Survival in Advanced Non-Small Cell Lung Cancer

Sudsawat Laohavinij MD, PhD\*, Jedzada Maneechavakajorn MD\*

\* Department of Medicine, Rajavithi Hospital

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**Objective :** To determine the prognostic value for survival of various pretreatment characteristics and treatments in advanced non-small cell lung cancer (NSCLC) patients.

**Patients and Method :** The retrospective study was conducted by reviewing the 81 files of advanced NSCLC patients treated with chemotherapy at the Oncology Unit, Rajavithi Hospital. Eighteen clinical variables were investigated and analysed as prognostic factors for survival.

**Results :** The first chemotherapy regimens for the 81 patients included: etoposide plus platinum derivatives (41), new drugs (taxanes or gemcitabine) plus platinum derivatives (39) and one other platinum based regimen (1). The overall survival time for all patients was 39.4 weeks with a 95% confidence interval of 30 to 49 weeks.

In the multivariate analysis, male gender, bone metastasis and liver metastasis are poor prognostic factors. Receiving palliative surgery and achieving objective response to first regimen chemotherapy are good prognostic factors. Patients who received either old or new drug combinations showed no difference in their survival as determined by univariate or multivariate analyses which could be due to limitations in the present retrospective study. However, this may show that regimens consisting of older, less expensive drug combinations still provide survival advantages in advanced NSCLC and should be considered in limited financial circumstances.

**Keywords :** Non-small-cell lung cancer (NSCLC), Chemotherapy, Prognostic factor

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Lung cancer in Thailand ranked second of ten leading sites of cancers in men in 1994 according to the Ramathibodi Cancer Registry<sup>(1)</sup>. Unfortunately, the majority of lung cancer patients present with inoperable stage III disease, or with metastatic disease (stage IV)<sup>(2)</sup>. Advanced non-small-cell lung cancer (NSCLC) has a median survival time of 6 to 8 months, and a 1-year survival rate of only 10% to 20%<sup>(3)</sup>. Although chemotherapy can effect a modest improvement in survival, the gain often comes with a substantial host toxicity, especially in patients who are less than fully ambulatory<sup>(4)</sup>. Cisplatin-containing chemotherapy regimens have led to only marginal improvement in survival<sup>(5)</sup>. A randomized trial conducted by the Eastern Co-operative Oncology Group<sup>(6)</sup> showed that single agent carboplatin, a cisplatin analogue which can be

easily given at the outpatient day care unit, significantly improved survival and produced significantly less toxicity than cisplatin-based combinations in stage IV NSCLC. Within the past 8 years, a number of new chemotherapeutic agents including vinorelbine, paclitaxel, docetaxel, gemcitabine, and topotecan have been identified that have shown a high degree of activity both as single agents, and in combination regimens against NSCLC. These new combination regimens have produced modest improvements in survival elsewhere<sup>(7)</sup>, though the cost of these new drugs is high. These observations prompted the authors to do a retrospective study of patients using various chemotherapy regimens with advanced non-small-cell lung cancer (NSCLC) in the Department of Medicine, Rajavithi Hospital to determine the prognostic value for progression free and overall survival of various pretreatment characteristics and treatments, especially the effect of new chemotherapy regimens.

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Correspondence to : Laohavinij S, Oncology Unit, Department of Medicine, Rajavithi Hospital, 2 Phyathai Road, Rajatevi, Bangkok 10400, Thailand. Phone: 0-2354-8059, Fax: 0-2354-8179

## Patients and Method

This retrospective study was conducted from selected medical files of patients with advanced NSCLC treated with platinum derivatives based chemotherapy in the Oncology Unit, at Rajavithi Hospital from June, 1995 to April, 2001. At enrollment in the unit, demographic and clinical data from each patient were systematically collected. Eighteen primary variables were collected, coded and entered into a computer statistical program. The 13 variables retrospectively studied as potential pretreatment prognostic variables included: age, sex, smoking (pack-years), WHO performance status, weight loss <10%/≥ 10%, dyspnea, presence of superior vena cava syndrome (SVCS), histologic type (squamous/non-squamous), TNM stage, and site of metastases (bone, lung, liver, adrenal gland). Five potential therapeutic prognostic variables also included in the analyses were type of first line chemotherapy regimen (new combination versus old combination), response to chemotherapy first regimen, number of chemotherapy regimens received, receiving palliative radiation and receiving palliative surgery.

Standard pretreatment work up included clinical evaluation, laboratory studies (complete blood count, biochemistry), radiologic evaluation (chest radiographs, chest and abdominal computed tomography (CT), bone isotope scanning, and ultrasonic examinations). Most patients received standard treatments based on disease stage, mainly stage IV. All chemotherapy schedules were cisplatin or carboplatin based regimens. Chemotherapy regimens could be divided in two groups: new third-generation regimens and conventional regimens. New third-generation regimens included cisplatin or carboplatin given with either paclitaxel or docetaxel or gemcitabine. Conventional regimens were cisplatin or carboplatin given with either etoposide or mitomycin C plus vinblastine. All patients were assessed for tumor response after the first regimen of chemotherapy. Some patients who had disease progression after first line chemotherapy and still had good performance status were offered additional second line chemotherapy regimens. Palliative radiation and surgery were given to patients having relevant indications.

Response evaluation was based on World Health Organization (WHO) criteria<sup>(8)</sup>. A complete response was defined as complete disappearance of all disease on radiographic and physical examination for a minimum of 4 weeks. Partial response was defined as a greater than 50% reduction in the sum of the

products of the perpendicular diameters of all measurable lesions for a minimum of 4 weeks. Stable disease was defined as no detectable change in the tumor volume of all the lesions. Progressive disease was defined as a greater than 25% increase in the sum of the products of the perpendicular diameters of all the measurable lesions or by the appearance of new lesions. All patients enrolled were monitored for treatment related toxicity, response, time to response, site of response, time to progression and time to death. Time to progression and survival were calculated from the date of entry into the study. Time to progression was defined as time to disease progression or time to death in absence of disease progression. Time to death was defined as time to death or last follow up.

## Statistical analysis

Progression-free survival and overall survival time were estimated using the method of Kaplan and Meier<sup>(9)</sup>. Eighteen variables were included for analyses to identify prognostic factors for survival. Comparisons of cumulative survival were obtained by univariate analyses using the log-rank test<sup>(10)</sup> and multivariate analyses were performed using Cox regression analysis.

## Results

### *Outcome of the treatment for the entire group*

From June 1995 through April 2001, 81 advanced NSCLC patients, treated with platinum derivatives based chemotherapy, were analysed. The characteristics of the 81 patients are listed in Table 1. There were 54 men and 27 women, with a median age of 63 years and a median ECOG PS of 2. Sixty nine percent of them lived in Bangkok and its surroundings. Sixty eight percent of the patients were smokers, of whom 47% smoked ≥ 20 pack-year. Thirty percent of the patients had weight loss ≥ 10%. Forty eight percent of the patients had dyspnea. Three-fourths of the patients had stage IV disease. The predominant histology was adenocarcinoma (60.5%). Most common site of metastasis was bone (47%).

The common first chemotherapy regimens with a median of 6 cycles included a combination of etoposide and carboplatin or cisplatin, 41 patients (51%), paclitaxel and carboplatin or cisplatin, 25 patients (31%), gemcitabine and carboplatin or cisplatin, 13 patients (16%) (Table 2, Table 3). Most patients received only one regimen of chemotherapy (69%), the rest received a second line of chemotherapy since they showed good performance status (ECOG

**Table 1.** Patient Characteristics

| Characteristics                 | No.       | (%)  |
|---------------------------------|-----------|------|
| Number of patient               | 81        |      |
| Age (years)                     |           |      |
| Median (range)                  | 63(29-84) |      |
| Sex                             |           |      |
| Male                            | 54        | 67   |
| Female                          | 27        | 33   |
| Location                        |           |      |
| Bangkok & surroundings          | 56        | 69   |
| Other                           | 25        | 31   |
| Smoking                         |           |      |
| None                            | 26        | 32   |
| 1-10 pack-year                  | 3         | 4    |
| 11-20 pack-year                 | 14        | 17   |
| >20 pack-year                   | 38        | 47   |
| ECOG performance status         |           |      |
| 0                               | 1         | 1    |
| 1                               | 29        | 36   |
| 2                               | 44        | 54   |
| 3                               | 7         | 9    |
| Pretreatment weight loss        |           |      |
| <10%                            | 57        | 70   |
| ≥10%                            | 24        | 30   |
| Dyspnea                         | 39        | 48   |
| Superior vena cava syndrome     | 2         | 3    |
| Histology                       |           |      |
| Squamous cell carcinoma         | 21        | 26   |
| Adenocarcinoma                  | 49        | 60.5 |
| Bronchoalveolar                 | 7         | 8.5  |
| Poorly differentiated carcinoma | 3         | 4    |
| Large cell carcinoma            | 1         | 1    |
| Other                           | 7         | 8.5  |
| Stage                           |           |      |
| IIIA (2) & IIIB (20)            | 22        | 27   |
| IV                              | 59        | 73   |
| Sites of Metastasis             |           |      |
| Bone                            | 38        | 47   |
| Contralateral lung              | 27        | 33   |
| Liver                           | 12        | 15   |
| Adrenal gland                   | 4         | 5    |

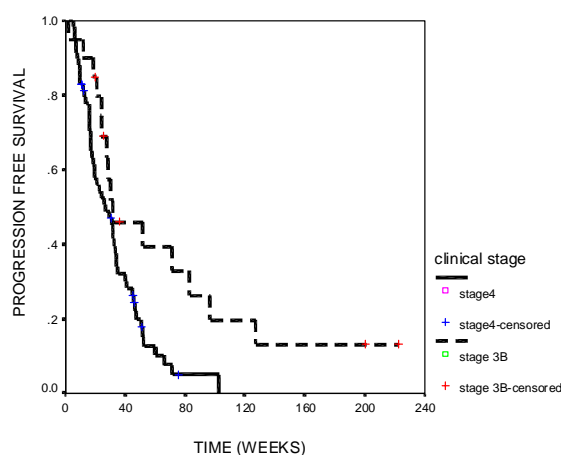
performance status 0-2). Palliative surgery and palliative radiation were given to 12 patients (15%) and 32 patients (40%) respectively (Table 3).

The objective response rate for the regimen of etoposide and platinum derivatives was 27% with 22% partial response and 5% complete response; 41% stable disease and 32% progressive disease after two cycles (Table 2). Patients receiving taxanes and platinum derivatives had an objective response rate of 42% with 38% partial response and 4% complete response; 35% stable disease and 23% progressive disease after two cycles. Gemcitabine and platinum

derivatives regimens had an objective partial response rate of 38.5%; 38.5% stable disease and 23% progressive disease after two cycles.

Second line chemotherapy was given to 25 patients (31%) and the regimens included new drug combinations in 13 patients and old drug combinations in 12 patients (Table 4). Objective responses were found in 3 patients receiving second line chemotherapy with one complete response in a patient receiving paclitaxel and carboplatin and 2 partial response in patients receiving etoposide plus platinum derivatives. Nine patients who received first line old drug combinations and 4 patients who received first line new drug combinations received second line new drug combinations.

The median progression free survival time for all 81 patients was 26 weeks with a 95% CI of 19 to 33 weeks. The median progression free survival time in patients with stage IIIB was 32 weeks (95% CI, 2-61 weeks) compared with 27 weeks (95% CI, 16-38 weeks) for stage IV patients, a statistically significant difference between the two groups ( $p = 0.016$ ) (Fig 1). At a median follow up time of 37 weeks (range 5-223 weeks), the median survival time for all 81 patients was 39.4 weeks (95% CI, 30 to 49 weeks). The 1-year survival rate was 44% (95% CI, 30% to 52%), and the 2-year survival rate was 14% (95% CI, 6% to 22%). Patients with stage IIIB had a significantly longer median survival time [77 weeks (95% CI, 60-95 weeks)] when compared with those who had stage IV disease [median survival 34 weeks (95% CI, 30-39 weeks),  $p = 0.003$ ; Fig 2].



**Fig. 1** Median progression free survival time, defined as freedom from disease progression or death from other causes for stage III B and stage IV patients was 32 weeks (95% CI 2-61 weeks) and 27 weeks (95% CI 16-38 weeks), respectively ( $p = 0.016$ )

**Table 2.** Clinical responses and survival time of 81 patients receiving different first chemotherapy regimens

| Regimen                               | No. (%) | Response no (%) |          |          |         | MST*(wk)<br>(95% CI) |
|---------------------------------------|---------|-----------------|----------|----------|---------|----------------------|
|                                       |         | CR              | PR       | SD       | PD      |                      |
| Etoposide + platinum <sup>(a)</sup>   | 41 (51) | 2 (5)           | 9 (22)   | 17 (41)  | 13 (32) | 37 (12-61)           |
| <sup>(b)</sup> Taxanes + platinum     | 26 (32) | 1 (4)           | 10 (38)  | 9 (35)   | 6 (23)  | 41 (29-52)           |
| Gemcitabine + platinum <sup>(c)</sup> | 13 (16) | -               | 5 (38.5) | 5 (38.5) | 3 (23)  | 36 (28-44)           |
| Mitomycin C/vinblastine/ cisplatin    | 1 (1)   | -               | -        | 1        | -       | 46                   |
| Old combination regimens              | 42 (52) | -               | -        | -        | -       | 37 (16-58)           |
| New combination regimens              | 39 (48) | -               | -        | -        | -       | 41 (29-52)           |

**Note** Abbreviation: MST, estimated median survival time; CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease

\* = Comparison of the median survival time between treatment groups shows no statistically significant difference

(a) = Carboplatin (34); Cisplatin (7)

(b) = Paclitaxel + Carboplatin(24); Paclitaxel + Cisplatin(1); Docetaxel + Cisplatin(1) (c) = Carboplatin (11); Cisplatin (2)

**Table 3.** Details of treatment

| Treatment   | No.      | (%) |
|---|----------|-----|
| Chemotherapy  |          |     |
| Number of chemotherapy regimen received                 |          |     |
| 1 regimen   | 56       | 69  |
| 2 regimens  | 21       | 26  |
| > 2 regimens  | 4        | 5   |
| Number of courses of first chemotherapy: median (range) | 6 (1-14) |     |
| Palliative surgery                                      | 12       | 15  |
| Palliative radiation                                    | 32       | 40  |

The median survival times for patients receiving different first line chemotherapy regimens were as follows: 37 weeks (95% CI, 12-61 weeks) for etoposide plus platinum derivatives; 41 weeks (95% CI, 29-52 weeks) for taxanes plus platinum derivatives; 36 weeks (95% CI, 28-44 weeks) for gemcitabine plus

platinum derivatives; and 46 weeks for the MVP regimen. The comparisons of median survival time of patients receiving different first line chemotherapy regimens using the log-rank test showed no significant difference between the groups. The patients were also grouped to include old combination chemotherapy regimens (etoposide plus platinum derivatives and MVP regimens) and new combination chemotherapy regimens (taxanes or gemcitabine plus platinum derivatives) and the cumulative survivals were compared using the log-rank test. The results also showed no significant difference in survival of patients receiving old or new combination chemotherapy regimens with a median survival time of 37 weeks (95% CI, 16-58 weeks) versus 41 weeks (95% CI, 29-52 weeks). Details of the median survival time of different treatment groups are listed in Table 2. Additionally, the 1-year survival rate for patients receiving old combination chemotherapy regimens was 40% (95%

**Table 4.** Clinical responses and survival time of 25 patients receiving various second line chemotherapy regimens

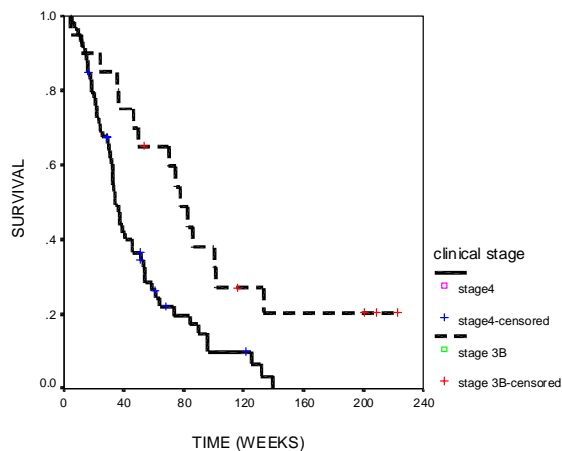
| Regimen                              | No. (%) | Response no (%) |        |         |        | MST(wk)<br>(95% CI) |
|--------------------------------------|---------|-----------------|--------|---------|--------|---------------------|
|                                      |         | CR              | PR     | SD      | PD     |                     |
| Paclitaxel + platinum <sup>(a)</sup> | 9 (36)  | 1 (11)          | -      | 1 (11)  | 7 (78) | 53 (8-98)           |
| Gemcitabine + carboplatin            | 1 (4)   | -               | -      | 1 (100) | -      | -                   |
| Etoposide + platinum <sup>(b)</sup>  | 8 (32)  | -               | 2 (25) | -       | 6 (75) | 70 (21-119)         |
| Other regimens <sup>(c)</sup>        | 7 (28)  | -               | -      | 1 (14)  | 6 (86) | 62 (24-99)          |

**Note** Abbreviation: MST, estimated median survival time; CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease

(a) = Carboplatin (7); Cisplatin (2)

(b) = Carboplatin(2); Cisplatin(7)

(c) = Docetaxel (2); Gemcitabine (1); Mitomycin C/vinblastine/ cisplatin (1) with SD; Other old drug combination (3)



**Fig. 2** Overall survival curve, median survival time for stage III B and stage IV patients was 77 weeks (95% CI, 60-95 weeks) and 34 weeks (95% CI, 30-39 weeks), respectively ( $p = 0.003$ )

CI, 25% to 55%) compared to 33% (95% CI, 18% to 48%) for patients receiving new combination chemotherapy regimens. Again, there was no statistically significant difference between the old and new regimen groups ( $p = 0.647$ ).

#### Univariate analyses

The authors collected pretherapeutic, therapeutic and clinical response data for 81 patients. Descriptive results from the 18 variables analyzed as potential prognostic factors are listed in Table 5.

Univariate survival analysis showed that WHO performance status  $< 2$ ; clinical stage III B; achieving complete or partial response to the first regimen of chemotherapy were highly significant prognostic factors for longer survival ( $p$  value  $< 0.005$ , log-rank test). Details of results are listed in Table 6. Other variables that were also associated with longer survival ( $p$  value between 0.01-0.05, log-rank test) were the absence of dyspnea at presentation, absence of liver and bone metastasis, and having palliative surgical treatment. The other tested variables, age, sex, smoking, presence of weight loss, presence of SVC syndrome, histology, presence of lung or adrenal metastasis, type of chemotherapy regimen (old regimens versus new regimens), number of chemotherapy regimens received and receiving palliative radiation therapy were not significantly associated with shorter or longer survival.

#### Multivariate analyses

The survival duration was further modeled with a multivariate Cox regression analysis employing

**Table 5.** Descriptive results

| Variables                                | Categories                | No. of Patients |
|--|---------------------------|-----------------|
| Age                                      | $< 60$ yr/ $\geq 60$ yr   | 31/50           |
| Sex                                      | male/female               | 54/27           |
| Smoking                                  | $\leq 20$ p-y/ $> 20$ p-y | 43/38           |
| PS                                       | $\leq 2$ / $> 2$          | 74/7            |
| Weight loss                              | $< 10\%$ / $\geq 10\%$    | 57/24           |
| Dyspnea                                  | no/yes                    | 42/39           |
| SVC syndrome                             | no/yes                    | 79/2            |
| Histology                                | squamous/<br>non-squamous | 21/60           |
| Stage                                    | III B/IV                  | 20/59           |
| Bone metastasis                          | no/yes                    | 43/38           |
| Lung metastasis                          | no/yes                    | 54/27           |
| Liver metastasis                         | no/yes                    | 69/12           |
| Adrenal metastasis                       | no/yes                    | 77/4            |
| Chemotherapy (1 <sup>st</sup> regimen)   | (new/old)                 | 39/42           |
| Response to CT (1 <sup>st</sup> regimen) | CR+PR/SD/PD               | 27/32/22        |
| Number of CT Regimen                     | 1/2/ $> 2$                | 56/21/4         |
| Surgery                                  | no/yes                    | 69/12           |
| Radiation                                | no/yes                    | 49/32           |

**Note** Abbreviation: p-y, pack-year; PS, WHO performance status; SVC, superior vena cava; CT, chemotherapy; CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease

**Table 6.** Significant variables determined by univariate survival analysis

| Variables                              | Categories | No. | MST (week) | $p^*$      |
|--|------------|-----|------------|------------|
| PS                                     | $\leq 2$   | 74  | 46         | 0.0003     |
|  | $> 2$      | 7   | 21         |            |
| Dyspnea                                | No         | 42  | 46         | 0.0412     |
|  | Yes        | 39  | 37         |            |
| Stage                                  | III B      | 20  | 77         | 0.003      |
|  | IV         | 59  | 34         |            |
| Liver metastasis                       | No         | 69  | 43         | 0.0135     |
|  | Yes        | 12  | 26         |            |
| Bone metastasis                        | No         | 43  | 54         | 0.0134     |
|  | Yes        | 38  | 33         |            |
| Response to first chemotherapy regimen | CR+PR      | 27  | 77         | $< 0.0001$ |
|  | SD         | 32  | 37         |            |
|  | PD         | 22  | 21         |            |
| Surgery                                | No         | 69  | 37         | 0.03       |
|  | Yes        | 12  | 46         |            |

**Note** Only significant variables ( $p < 0.05$ ) are listed here,  $p =$  two-sided significance probability for the log-rank test  
Abbreviation: MST, estimated median survival time; PS, WHO performance status; CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease

+ Log-rank test

a proportional hazard rate hypothesis. The 18 variables for this analysis are listed in Table 5. Pretherapeutic variables included: age, sex, smoking (pack-years), WHO performance status, weight loss <10%/≥ 10%, dyspnea, presence of superior vena cava syndrome (SVCS), histologic type (squamous/non-squamous), TNM stage, and presence of metastases (bone or lung or liver or adrenal gland). Post-therapeutic variables included: type of first chemotherapy regimen, responses to first chemotherapy regimen, number of chemotherapy regimens, and treatment with palliative radiation or palliative surgery. The results of multivariate survival analysis are described in Table 7. Sex (female) ( $p = 0.0414$ ), bone metastasis ( $p = 0.0272$ ) and liver metastasis ( $p = 0.0004$ ) were pretherapeutic independent predictors for survival. Female patients showed better survival compared to males with a relative risk of 0.49. Patients with bone and liver metastasis had a poorer survival compared to patients who did not have metastasis (relative risks of 2.31 and 6.36 respectively). For post-therapeutic predictors, response to the first chemotherapy regimen and surgical intervention were independent predictors. Patients who achieved stable disease or progressive disease had a poorer survival compared with those who achieved objective responses after the first chemotherapy regimen (relative risk of 3.24 and 20.35 respectively). Palliative surgical intervention was also found to be a protective predictor with a relative risk of 0.24.

## Discussion

In the present study, the authors observed a favorable median survival time for all 81 patients of 39.4 weeks (95% CI, 30 to 49 weeks). The 1-year and 2-year survival rates were 44% (95% CI, 30% to 52%), and 14% (95% CI, 6% to 22%) respectively. The present results are encouraging and compare favorably

with response rates and survival results following cisplatin based chemotherapy in other studies<sup>(5,7)</sup>. Patients with stage IIIB had a significantly longer median survival time when compared with those who had stage IV disease (77 weeks versus 34 weeks). The patients receiving new combination regimens (48% of cases) had a favorable objective response rate when compared with etoposide plus carboplatin (51% of cases) 38-42 % versus 27%. However, median survival time and 1-year survival rate of patients receiving both old and new combination regimens were not statistically significant different, that is, 37 weeks versus 41 weeks and 40% versus 33%.

The results of other randomized phase III studies<sup>(11-13)</sup> in advanced NSCLC that compared new two-drug combinations (paclitaxel/cisplatin, gemcitabine/cisplatin, docetaxel/ciplatin) with an old cisplatin based two-drug combination showed an advantage for the new combination with respect to efficacy and toxicity. But the advantages were often modest and survival differences were not consistently statistically significant<sup>(11-13)</sup>. Le Chevalier et al<sup>(14)</sup> and Bonomi et al<sup>(15)</sup> conducted randomized trials that showed the new drug combinations produced higher response rates and significantly superior survival compared with the older combinations (Table 8). However, in the last of these studies<sup>(15)</sup> quality of life scores of patients were not significantly different among the regimens. The results of phase III randomized trials discussed above have shown either no or modest improvement in survival with the use of newer chemotherapy regimens. When the present results were compared with others, the authors found no survival advantages from using first line, new third drug generation combinations for advanced NSCLC patients while other studies found a modest improvement in survival. This could be due to small patient numbers, a limitation of the present retrospective study. In addition, 9 patients (11%) in

**Table 7.** Significant variables determined by multivariate survival analysis

| Variables                              | Coeff. | SE   | RR    | 95% CI     | p       |
|--|--------|------|-------|------------|---------|
| Sex (F)                                | -0.71  | 0.35 | 0.49  | 0.25-0.97  | 0.0414  |
| Bone metastasis (yes)                  | 0.84   | 0.38 | 2.31  | 1.10-4.85  | 0.0272  |
| Liver metastasis (yes)                 | 1.85   | 0.52 | 6.36  | 2.28-17.75 | 0.0004  |
| Response to first chemotherapy regimen |        |      |       |            |         |
| SD                                     | 1.18   | 0.43 | 3.24  | 1.40-7.48  | 0.0058  |
| PD                                     | 3.01   | 0.62 | 20.35 | 6.02-68.70 | <0.0001 |
| Surgery (yes)                          | -1.43  | 0.51 | 0.24  | 0.09-0.65  | 0.0049  |

**Note** Abbreviation: SD, stable disease; PD, progressive disease  
(Coeff: coefficient, SE: standard error, RR: relative risk, 95%CI: 95% confidence interval)

**Table 8.** Results of randomized trials of standard chemotherapy combinations versus new chemotherapy combinations

| Author                       | Regimen                   | RR (%) | MST (wk) | 1-year S (%) | p     |
|------------------------------|---------------------------|--------|----------|--------------|-------|
| Le Chevalier <sup>(14)</sup> | Vinorelbine/<br>cisplatin | 44     | 50       | 40           | 0.04  |
|                              | Vindesine/<br>cisplatin   | 32     | 46       | 32           |       |
| Bonomi <sup>(15)</sup>       | Paclitaxel/<br>cisplatin  | 27.7   | 40       | 38.9         | 0.048 |
|                              | Etoposide/<br>cisplatin   | 12.4   | 30       | 31.8         |       |

**Note** Abbreviation: MST, estimated median survival time; 1-year S, 1-year survival; RR, response rate

this study who received older drug combinations as first line chemotherapy, received new drug regimens in further second line treatment. This could affect the survival of patients in the old drug combination groups and result in no survival difference between patients receiving old versus new drug combination regimens in the present study. Based on the present result, the authors conclude that regimens consisting of old drug combinations, especially etoposide plus platinum derivatives, have benefit and provide survival advantages in advanced NSCLC patients.

In addition, a recently reported meta-analysis of the published literature<sup>(16)</sup> comparing platinum-based regimens including a new third-generation agent to older platinum-based regimens demonstrated that 1-year survival and response rates were increased for patients receiving new third-generation regimens, with an absolute average increase of 4% and 13% respectively. At present, results of phase III studies and meta-analysis suggest that there has been a significant, albeit small improvement in survival with the use of new chemotherapy regimens compared to the older regimens. The advantages of new two-drug combinations were more often in toxicity, quality of life and convenience, though meta-analysis has shown a significant but small improvement in survival. In Thailand, where cost is an important factor, older two-drug combinations show comparable long-term effectiveness and should be considered useful chemotherapy regimens in advanced NSCLC.

In the literature, most of the studies searching for prognostic factors of NSCLC have been based on clinical characteristics, histological studies and tumor markers<sup>(17-20)</sup>. Prognostic factors of advanced NSCLC which have also been studied in order to identify

selected advanced NSCLC patients for systemic therapy included performance status, weight loss, sex, age, symptoms, stage, number and sites of metastasis and treatment<sup>(21)</sup>.

Consistent with a previous report on prognostic factors in advanced NSCLC<sup>(17)</sup>, multivariate analysis in the present study identified liver metastases as a factor adversely influencing survival, as was bone metastasis. Female gender, achieving objective responses from chemotherapy or palliative surgery were positively associated with survival, as also confirmed by previous reports<sup>(17,19)</sup>. The present study also showed that response to treatment is also an important prognostic factor for survival. This confirms the results from previous phase II studies which have shown that responding, advanced NSCLC patients treated with cisplatin and etoposide or MIC or MVP regimens survived significantly longer than non responders<sup>(22-24)</sup>. Performance status (PS) has been the most important prognostic factor for survival in many studies<sup>(17-19)</sup>. In the present study, multivariate analysis did not show PS an independent prognostic factor. This could be due to the small number of patients compared with other studies. However, univariate analysis in the present study showed patients with a PS to be less than or equal to 2 had better survival when compared with patients with a PS greater than 2. As PS is a consistent prognostic factor for survival for advanced NSCLC, it is recommended that PS be used to select patients for systemic chemotherapy<sup>(21)</sup>. In other studies<sup>(17-20)</sup>, age, weight loss and dyspnea were also inconsistent prognostic factors as in the present results.

In conclusion, the present study showed that gender, presence of bone metastasis, presence of liver metastasis, response to first chemotherapy regimen and palliative surgical intervention are independent prognosticators of survival in patients with advanced stage NSCLC treated with chemotherapy. The present study found no survival advantages from using first line new drug combinations. This could be due to limitations of this retrospective study, but does not diminish the fact that old drug regimen combinations still have survival advantages in advanced NSCLC.

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## ปัจจัยพยากรณ์ที่มีผลต่อการรอดชีพของผู้ป่วยโรคมะเร็งปอดชนิด Non-Small Cell ระยะลุกลาม

สุดสวาท เลหาวิณีจ, เจษฎา มณีชวขจร

**วัตถุประสงค์ :** เพื่อศึกษาหาปัจจัยพยากรณ์ที่มีผลต่อการรอดชีพของผู้ป่วยมะเร็งปอดชนิด Non-Small Cell (NSCLC) โดยศึกษาวิเคราะห์ปัจจัยก่อนการรักษาและวิธีการรักษาผู้ป่วย

**การศึกษา :** เป็นการศึกษาแบบย้อนหลังเวชระเบียนของผู้ป่วย NSCLC ระยะลุกลามจำนวน 81 ราย ที่รับการรักษาด้วยยาเคมีบำบัด ณ งานโรคมะเร็ง กลุ่มงานอายุรกรรม โรงพยาบาลราชวิถี โดยวิเคราะห์ 18 ปัจจัยที่อาจพยากรณ์การรอดชีพของผู้ป่วย

**ผลการศึกษา :** สูตรยาเคมีบำบัดสูตรแรกที่ได้รับได้แก่ Etoposide ร่วมกับ Platinum derivatives 41 ราย ยาใหม่ (taxanes หรือ gemcitabine) ร่วมกับ platinum derivatives 39 ราย และสูตร platinum based อื่น 1 ราย ระยะเวลาการรอดชีพของผู้ป่วยทั้งหมดเท่ากับ 39.4 สัปดาห์ โดยมีค่า 95% confidence interval เท่ากับ 30 ถึง 49 สัปดาห์ การวิเคราะห์ชนิด multivariate พบว่าเพศชาย, การกระจายของโรคที่กระดูกและการกระจายของโรคที่ตับเป็นปัจจัยพยากรณ์โรคที่ไม่ดี ขณะที่การได้รับการผ่าตัดเพื่อการประคับประคองและการตอบสนองต่อการรักษาด้วยยาเคมีบำบัดสูตรแรกเป็นปัจจัยพยากรณ์โรคที่ดี ผู้ป่วยที่รับการรักษาด้วยยาเคมีบำบัดสูตรเก่าหรือสูตรใหม่ มีระยะเวลาการรอดชีพไม่แตกต่างกันซึ่งอาจเป็นผลจากข้อจำกัดของวิธีการศึกษาที่เป็นการศึกษาแบบย้อนหลัง จากการศึกษานี้แสดงให้เห็นว่าสูตรยาเคมีบำบัดที่ประกอบด้วยยาเก่าซึ่งราคาเยอแม้ว่าจะยังมีประสิทธิภาพในการเพิ่มระยะเวลาของการรอดชีพของผู้ป่วย NSCLC ระยะลุกลาม

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