

# Survival of Patients with Advanced Non-Small Cell Lung Cancer in Chonburi Cancer Hospital

Suhauchai S

Chonburi Cancer Hospital, Samet, Mueang Chon Buri, Chonburi, 20000

(E-mail : maxstmdcu@yahoo.com)

บทคัดย่อ : การรอดชีพในผู้ป่วยมะเร็งปอดชนิด Non-Small Cell

ระยะลุกลามในโรงพยาบาลมะเร็งชลบุรี

สิกธิ สุขวิชัย ผ.บ.

โรงพยาบาลมะเร็งชลบุรี ตำบลเสเม็ด อำเภอเมือง จังหวัดชลบุรี 20000

**วัตถุประสงค์ :** เพื่อศึกษาการรอดชีพในผู้ป่วยมะเร็งปอดระยะลุกลาม ในผู้ป่วยที่รับการรักษาที่โรงพยาบาลมะเร็งชลบุรี และประเมินคุณภาพการบริบาลผู้ป่วยมะเร็ง รวมถึงหน้าปัจจัยการพยากรณ์โรคในผู้ป่วยมะเร็งปอดระยะลุกลาม **วิธีการ :** เป็นการศึกษาข้อมูล โดยการทบทวนวรรณเวชระเบียนผู้ป่วยที่ได้รับการรินิจชัยเป็นมะเร็งปอดชนิด non-small cell ระยะที่ IIIB-IV ที่ได้รับรักษาที่หน่วยเคมีบำบัด โรงพยาบาลมะเร็งชลบุรี ในช่วงวันที่ 1 กรกฎาคม พ.ศ. 2556 ถึง 30 มิถุนายน พ.ศ. 2558 ผล : พบรู้ป่วยจำนวน 94 ราย ค่ามัธยฐานของอายุอยู่ที่ 61 ปี ค่ามัธยฐานการรอดชีพของผู้ป่วยทั้งหมดอยู่ที่ 8.62 เดือน โดยค่ามัธยฐานการรอดชีพของผู้ที่ได้รับยา.rักษาเทียบกับกลุ่มที่ไม่ได้รับยาอยู่ที่ 10.60 เดือน และ 4.17 เดือน ตามลำดับ ( $p<0.001$ ) มีผู้ป่วยพึงร้อยละ 12.5 ที่ได้รับการตรวจ EGFR mutation ด้านคุณภาพการบริบาลผู้ป่วยตามบันทึกเวชระเบียน พบว่าผู้ป่วยบางรายไม่ได้รับทราบการพยากรณ์เกี่ยวกับโรค ผู้ป่วยบางรายไม่ได้รับการดูแลจากการหนีอยหรืออาการปวดอย่างเหมาะสม และผู้ป่วยบางรายไม่ได้รับการบันทึกสภาพความแข็งแรงของร่างกาย (ECOG performance status) ก่อนได้รับการตัดสินใจรักษา ด้านปัจจัยพยากรณ์โรค วิเคราะห์โดย Multivariate พบรู้ป่วยที่มีสภาพร่างกายไม่แข็งแรง ECOG 2-4 ( $p<0.001$ ) ไม่ได้รับการบันทึกสภาพร่างกายก่อนการรักษา ( $p=0.001$ ) และผู้ป่วยที่มีมะเร็งกระจายไปที่เยื่อหุ้มปอด ( $p=0.017$ ) เป็นปัจจัยการพยากรณ์โรคที่ไม่ได้ต่อการรอดชีพ **สรุป :** การรอดชีพของผู้ป่วยมะเร็งปอดระยะลุกลามที่รักษาที่โรงพยาบาลมะเร็งชลบุรีเที่ยบเท่าการศึกษาอื่นๆ การบริบาลผู้ป่วยมะเร็งและการรักษาแบบประคับประคองจำเป็นต้องได้รับการพัฒนาในโรงพยาบาล

เพื่อเพิ่มคุณภาพการดูแลผู้ป่วย และพบว่าผู้ป่วยที่มีสภาพร่างกายไม่ดี การไม่ได้รับการบันทึกสภาพร่างกาย และการมีมะเร็งกระจายไปเยื่อหุ้มปอดเป็นปัจจัยการพยากรณ์โรคที่ไม่ได้ต่อการรอดชีพ

**คำสำคัญ :** มะเร็งปอดชนิด Non-small cell การรอดชีพ คุณภาพการบริบาล ปัจจัยการพยากรณ์โรค

## Abstract

**Objectives :** To study a survival of patients with advanced non-small cell lung cancer treated in Chonburi Cancer Hospital. A quality of care in the hospital and prognostic factors for survival in these patients were also assessed. **Methods :** This retrospective cohort study was performed by reviewing 94 medical records of stage IIIB-IV non-small cell lung carcinoma patients cared in Chemotherapy unit, Chonburi Cancer Hospital from July 1<sup>st</sup> 2013 to June 30<sup>th</sup> 2015. **Results :** There were 94 patients whose median age were 61 years. The median survival time of all patients was 8.62 months. Median survival times of patients receiving systemic therapy and not receiving systemic therapy were 10.60 months and 4.17 months, respectively ( $p<0.001$ ). The small number of patients (12.5%) were tested for epidermal growth factor receptor (EGFR) mutation status. For quality cancer care aspects, according to medical records, we found that not all patients were informed about their diseases, appropriate care for their pains and difficulties of breath.

Some patients were not recorded their Eastern cooperative oncology group (ECOG) performance status before decisions of physicians for treatments. Multivariate analysis showed that the ECOG performance status 2-4 ( $p<0.001$ ), no record for ECOG performance status ( $p=0.001$ ) and pleural metastasis ( $p=0.017$ ) were significantly unfavorable prognostic factors for the survival. **Conclusion :** The survival time of advanced non-small cell lung carcinoma of our patients was comparable to other studies. A development in the palliative care and other aspects of quality cancer care were necessary for patient care improvement. The poor ECOG performance status, no record for ECOG performance status and having pleural metastasis were poor prognostic factors for the overall survival.

**Keywords :** Non-small cell lung cancer, Survival, Quality cancer care, Prognostic factor.

## Introduction

In 2012, lung carcinoma was the third most common cancer in the world<sup>1</sup>, after prostate and breast cancers, respectively. Lung carcinoma, however, was the most common cause of death in cancer around the world. In Thailand, at the same time, lung carcinoma was the third most common cancer after breast and hepatobiliary malignancies, but it was the second cause of death in cancer after hepatobiliary malignancy. In the same year, at Chonburi Cancer Hospital (CCH)<sup>2</sup>, lung cancer was again the third most common cancer after breast and cervical cancers, nevertheless, it was the most common cancer in male.

More than two decades, a standard treatment of patients with stage IIIB-IV non-small cell lung carcinoma has been a platinum-based chemotherapy which has been able to provide the median survival approximately 8-10 months<sup>3-5</sup>, moreover a developed regimen of therapy was more specific to types of patients' tumors such as a squamous or nonsquamous cell carcinoma<sup>6</sup>. However, a truly innovative therapy that opened a new era of the lung cancer treatment was an epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) studied by Mok<sup>7</sup>. This outstanding targeted therapy confirmed by a many later studies<sup>8-11</sup> needed to select more specific group of patients with positive epidermal growth factor

receptor (EGFR) mutation before giving them the EGFR-TKI in a first-line treatment and this therapy was able to provide median survival up to 20-30 months in these patients.

Nowadays, a standard recommendation for treatment<sup>12</sup> of patients with advanced stage non-small cell lung carcinoma primarily depends on an eastern cooperative oncology group (ECOG) performance status, a pathologic type of cancer, an EGFR status, an anaplastic lymphoma kinase (ALK) status. Nonetheless, in clinical practice, other factors need to be considered to make a decision to the treatment pathway such as patients' health funds, patients' preferences, meanwhile, the testing for EGFR and ALK statuses are not commonly done in clinical practice in CCH and may in Thailand.

This study intended to find the survival time of patients with advanced stage non-small cell lung carcinoma treated in CCH. Additionally, to evaluate quality of care in advanced cancer patients, we also paid attention to palliative care aspects such as a caring for pain, a caring for shortness of breath and an informing a patient to planning for his life and family. Besides, this study also aims to find prognostic factors for survival in the patients.

## Materials and Methods

This research was a retrospective study to in patients with non-small cell lung carcinoma stage IIIB-IV according to International Union Against Cancer (seventh edition)<sup>13</sup>, confirmed by histology as well as an imaging and treated at chemotherapy unit in CCH during the past 2 years, July 1<sup>st</sup> 2013 to June 30<sup>th</sup> 2015. All patients had to be followed to the date of December 31<sup>st</sup> 2015. A status of the patient at the cut point time was taken from the medical record and registration information, Ministry of Interior, Thailand. This study was approved by Ethics committee of CCH.

An overall survival time was calculated from the date of entry to the study to the date of death. Progression free survival time was calculated from the date of starting treatment to the date of tumor progression or death. Tumor responses were assessed using response evaluation criteria in solid tumors (RECIST) criteria<sup>14</sup> based on radiologic report (CT scan or plain-film) and physical examination.

Overall survival time was estimated using the method of Kaplan and Meier<sup>15</sup>. Fifteen variables were included for analyses to identify prognostic factors for overall survival. Comparisons of cumulative survival were obtained by univariate analyses using the log-rank test<sup>16</sup> and multivariate analyses were performed using Cox proportional hazard regression. A p-value<0.10 in univariate analysis and <0.05 in multivariate analysis were considered statistical significant. SPSS version 16.0 was used in this study.

## Results

From July 1<sup>st</sup> 2013 to June 30<sup>th</sup> 2015, one hundred eighteen medical files were selected to review. Twenty four files of patients were excluded because twenty patients also received systemic therapies from other hospitals and two patients were unclear in staging and the other two patients were diagnosed of small cell lung carcinoma. In sum, ninety four medical records of patients were actually included, reviewed and recorded their information to analyze. The data was cut off on December 31<sup>st</sup> 2015.

Patients' clinical characteristics were listed in Table 1. Median age was 61 years old (range 29-91). There were 59 males (62.8%) and 35 females (37.2%). Sixty one patients (64.9%) had current or former histories of tobacco smoking. Seventy eight (83%) and sixteen patients (17%) were diagnosed of stage IV and stage IIIB non-small cell lung carcinoma, respectively. The two most common histologic types were adenocarcinoma (76.6%) and squamous cell carcinoma (14.9%). The three most common presenting symptoms of the patients were cough (41.4%), dyspnea (18%) and chest pain (16%). An ECOG performance status was literally recorded by physicians in seventy patients (74.4%) at first visiting or before providing first-time systemic therapy. The three most common metastatic sites were pleura (36.1%), lung (31.9%) and bone (27.6%). Only nine patients (12.5%) and eight patients (11.1%) of adenocarcinoma patients were evaluated for EGFR mutation and ALK translocation statuses, respectively.

**Table 1 Patient characteristic**

| N=94                       | Number | %    |
|----------------------------|--------|------|
| Age, years                 |        |      |
| Median                     | 61     |      |
| Range                      | 29-91  |      |
| Sex                        |        |      |
| Male                       | 59     | 62.8 |
| Female                     | 35     | 37.2 |
| Health fund group*         |        |      |
| UCC                        | 63     | 67.0 |
| SCC                        | 18     | 19.1 |
| GSEO                       | 13     | 13.9 |
| Smoking                    |        |      |
| Former/current             | 61     | 64.9 |
| None                       | 33     | 35.1 |
| Stage                      |        |      |
| III-B                      | 16     | 17.0 |
| IV                         | 78     | 83.0 |
| Pathology                  |        |      |
| Adenocarcinoma             | 72     | 76.6 |
| Squamous cell carcinoma    | 14     | 14.9 |
| Poorly differentiation     | 3      | 3.2  |
| Others**                   | 5      | 5.3  |
| Tissue diagnosis           |        |      |
| Pathology                  | 78     | 82.9 |
| Cytology                   | 16     | 17.1 |
| ECOG*** performance status |        |      |
| 0-1                        | 35     | 37.2 |
| 2                          | 18     | 19.1 |
| 3-4                        | 17     | 18.1 |
| No record                  | 24     | 25.5 |

**Table 1 Patient characteristic (Continue)**

| N=94                         | Number | %    |
|------------------------------|--------|------|
| Presenting symptom           |        |      |
| Cough                        | 39     | 41.4 |
| Dyspnea                      | 17     | 18.0 |
| Chest pain                   | 15     | 16.0 |
| Brain metastasis             | 12     | 12.7 |
| Lymphadenopathy              | 5      | 5.3  |
| Bone metastasis              | 5      | 5.3  |
| SVC obstruction <sup>§</sup> | 3      | 3.2  |
| Others <sup>§§</sup>         | 17     | 18.1 |
| Metastatic site              |        |      |
| Pleura                       | 34     | 36.1 |
| Lung                         | 30     | 31.9 |
| Bone                         | 26     | 27.6 |
| Brain                        | 17     | 18.1 |
| Distant lymph node           | 12     | 12.7 |
| Liver                        | 11     | 11.7 |
| Adrenal gland                | 6      | 6.3  |
| Others <sup>§§§</sup>        | 10     | 10.6 |

\* UCC : Universal coverage scheme, SCC : Social security scheme, and GSEO : Government or State Enterprise Officer

\*\* no-other specifies 3, large cell carcinoma 1, adeno-squamous cell carcinoma 1

\*\*\*ECOG : Eastern cooperative oncology group

§ SVC : superior vena cava

§§ abnormal chest x-rays 4, pneumonia 3, hoarseness of voice 3, hemoptysis 3, no record 2, weight loss 1, dysphagia 1, abdominal pain 1; (a patient might presented with more than one symptoms)

§§§ meninges 4, pericardium 3, breast 1, paravertebral soft tissue 1, spleen 1

At the cut point of time on December 31<sup>st</sup> 2015, seventy two patients (76.5%) had died. On the other hand, twenty two patients who stayed alive, nine of whom were periodically appointed for following of imaging and their symptoms and were planned for further therapy if there was evidence of disease progression. In addition, systemic therapy and best-supportive care were given in three and seven patients, respectively. The other three patients lost to follow up.

First-line palliative systemic therapy was given to seventy two patients (Table 2) chemotherapy in 70 patients (stage IIIB 7, stage IV 63), EGFR-TKI in 2 patients. In sixteen patients with stage IIIB disease non-small cell lung carcinoma, seven patients received palliative chemotherapies (and/or a palliative radiotherapy) and five patients received concurrent chemo-radiotherapy (and/or induction chemotherapy), additionally, two of the five patients also received maintenance EGFR-TKI after concurrent chemo-radiotherapy. Two of sixteen patients received sequential chemo-radiotherapy and the other two received only best supportive care.

**Table 2 Number of systemic regimens in 72 patients receiving palliative systemic therapy**

| Chemotherapy   | Number | %   |
|----------------|--------|-----|
| 1 Regimen      | 72     | 100 |
| 2 Regimens     | 39     | 54  |
| 3 Regimens     | 14     | 19  |
| 4 Regimens     | 5      | 7   |
| Median regimen | 2      |     |

Seventy eight patients with stage IV disease, in first-line treatment, sixty three patients received palliative chemotherapy, two received EGFR-TKI, and the other two received only best supportive care. In patients receiving palliative chemotherapy, all of whom were treated by third-generation conventional platinum doublets, excepting for three patients received non-conventional platinum combination chemotherapy; one received single agent gemcitabine, another received cisplatin/etoposide, and the other received carboplatin/S-1. The median cycle of first-line palliative chemotherapy was four (range 1-6).

The commonly used chemotherapy regimens were carboplatin/paclitaxel and carboplatin/gemcitabine.

Second-line systemic therapies were given in thirty nine patients, twenty six of whom received docetaxel, seven of whom received EGFR-TKI, four of whom received conventional platinum doublets and the other two of whom received other platinum combinations (1 cisplatin/etoposide, 1 carboplatin/TS1). The median cycle of second-line palliative chemotherapy was three point five (range 1-6).

Third-line and fourth-line systemic therapies were provided in fourteen and five patients, respectively. Median regimen of systemic therapy was two (range 1-5).

Forty four patients received radiotherapy. The most common of radiotherapy was palliative whole brain radiation in twenty patients with brain metastasis. Palliative radiotherapy to bone and to mediastinum (and/or lung tumor) was provided in fifteen and ten patients, respectively. Seven patients received concurrent chemo-radiotherapy (five with stage IIIB and two with stage IV). The other two received sequential chemo-radiotherapy in stage IIIB disease.

According to the medical records, the prognosis of the disease was informed to the patients and their families in fifty-eight patients (61.7%). Difficulties in breathing and

cancer pains were recorded in forty-three patients (45.7%) and sixty-one patients (64.8%), respectively. In these patients, 43 out of 47 (91.4%) of breath difficulty patients and 59 out of 61 (96.7%) pain patients were actually cared for their symptoms.

### Response to systemic therapy

In the first-line systemic therapy, the overall response rate was 20.9% (14/67) in patients receiving palliative chemotherapy (Table 3) and 100% (2/2) in patients receiving EGFR-TKI. In the second-line chemotherapy, the overall response rate with docetaxel was 7.7% (2/26), but no response was found in patients receiving platinum doublets.

**Table 3. Response to systemic therapy**

| Chemotherapy              | Number | Response to chemotherapy <sup>#</sup> , Number |    |    |    |    |
|---------------------------|--------|--|----|----|----|----|
|                           |        | CR   | PR | SD | PD | NA |
| First-line                | 72     | 1  | 16 | 27 | 17 | 11 |
| Paclitaxel/Carboplatin    | 35     | 1  | 8  | 14 | 5  | 7  |
| Gemcitabine/Carboplatin   | 29     |  | 5  | 12 | 10 | 2  |
| Gemcitabine/Cisplatin     | 3      |  |    |    | 2  | 1  |
| Tyrosine kinase inhibitor | 2      |  | 2  |    |    |    |
| Others*                   | 3      |  | 1  | 1  |    | 1  |
| Second-line               | 39     | 0  | 2  | 16 | 17 | 4  |
| Docetaxel                 | 26     |  | 2  | 11 | 9  | 4  |
| Platinum doublets         | 4      |  |    | 3  | 1  |    |
| Tyrosine kinase inhibitor | 7      |  |    | 1  | 6  |    |
| Others**                  | 2      |  |    | 1  | 1  |    |
| Third-line                | 14     | 0  | 2  | 4  | 7  | 1  |
| Docetaxel                 | 3      |  |    | 1  | 1  | 1  |
| Gem/Carboplatin           | 2      |  |    | 1  | 1  |    |
| Tyrosine kinase inhibitor | 4      |  | 1  |    | 3  |    |
| Others***                 | 5      |  | 1  | 2  | 2  |    |
| Fourth-line               | 5      | 0  | 0  | 1  | 3  | 1  |
| Gemcitabine/Carboplatin   | 1      |  |    |    | 1  |    |
| Gemcitabine               | 2      |  |    |    | 2  |    |
| Tyrosine kinase inhibitor | 2      |  |    | 1  |    | 1  |

\* Carboplatin/S-1 (1PR), Gemcitabine (1SD), cisplatin/etoposide (1NA). \*\* Cisplatin/etoposide (1SD), Carboplatin/S-1 (1NA). \*\*\*

Carboplatin/Etoposide (1PR,1PD), Paclitaxel (2SD), Cisplatin/etoposide (1PD).<sup>#</sup> CR : complete response, PR : partial response, SD : stable disease, PD : progressive disease, NA : non-available data

Median overall survival time of all patients in this study was 8.62 months. In addition, overall survival time in patients receiving and those who not receiving systemic treatment was 10.60 months and 4.17 months, respectively. Furthermore, after excluding two patients received EGFR-TKI for first-line systemic therapy, overall survival and progression free survival times in patients receiving palliative chemotherapy were 9.50 and 4.51 months, respectively. Two patients who received EGFR-TKI as first-line systemic therapy have survival at 13.57 and 18.37 months, and progression free survival at 7.23 and 4.30 months, respectively. Both of these patients, however, had not been tested for EGFR mutation before receiving EGFR-TKI.

Univariate factors for survival were assessed by log-rank test (Table 4) and found that the favorable significant prognostic factors ( $p<0.10$ ) for survival were ECOG 0-1 ( $p<0.001$ ), health fund group B ( $p=0.031$ ), positive EGFR mutation status ( $p=0.061$ ), no pleural metastasis ( $p=0.040$ ), receiving systemic therapy ( $p<0.001$ ), receiving radiotherapy ( $p=0.033$ ). On the contrary, factors not contributing to significant for prognostic factor were age group, sex, receiving EGFR-TKI (data not show), smoking status, stage, adenocarcinoma, lung metastasis, brain metastasis, bone metastasis, liver metastasis.

**Table 4 Univariate analysis of plausible prognostic factors in stage IIIB-IV NSCLC**

| Factors                 | Number | Deaths | Median survival<br>(Month) | 95% CI     | p-value |
|-------------------------|--------|--------|----------------------------|------------|---------|
| All patients            | 94     | 72     | 8.62                       | 1.00-22.51 |         |
| Age                     |        |        |                            |            |         |
| ≤70                     | 65     | 51     | 8.04                       | 5.74-10.34 | 0.599   |
| >70                     | 29     | 21     | 10.70                      | 7.58-13.83 |         |
| Sex                     |        |        |                            |            |         |
| Male                    | 59     | 44     | 10.14                      | 7.34-12.93 | 0.761   |
| Female                  | 35     | 28     | 8.70                       | 5.84-11.55 |         |
| ECOG performance status |        |        |                            |            |         |
| 0-1                     | 35     | 22     | 12.67                      | 7.60-17.73 | <0.001  |
| 2-4                     | 35     | 31     | 6.77                       | 4.84-8.69  |         |
| No record               | 24     | 19     | 5.74                       | 1.97-9.50  |         |
| Smoking status          |        |        |                            |            |         |
| Never                   | 33     | 26     | 10.34                      | 5.11-15.56 | 0.831   |
| Current/former          | 61     | 46     | 8.55                       | 6.03-11.04 |         |
| Health fund*            |        |        |                            |            |         |
| Group A                 | 81     | 65     | 8.30                       | 5.92-10.67 | 0.031   |
| Group B                 | 13     | 7      | 13.80                      | 9.60-17.99 |         |
| Stage                   |        |        |                            |            |         |
| III-B                   | 16     | 11     | 10.70                      | 5.40-15.99 | 0.216   |
| IV                      | 78     | 61     | 8.70                       | 6.21-11.18 |         |
| Adenocarcinoma          |        |        |                            |            |         |
| Yes                     | 72     | 53     | 9.50                       | 7.46-11.53 | 0.104   |
| No                      | 22     | 19     | 5.74                       | 1.60-9.87  |         |

Table 4 Univariate analysis of plausible prognostic factors in stage IIIB-IV NSCLC (Continue)

| Factors              | Number | Deaths | Median survival<br>(Month) | 95% CI     | p-value |
|----------------------|--------|--------|----------------------------|------------|---------|
| EGFR mutation status |        |        |                            |            |         |
| Positive             | 5      | 2      | 22.87                      | 9.68-36.05 | 0.061   |
| Negative             | 4      | 3      | 6.00                       | 0.00-12.76 |         |
| Unknown              | 85     | 67     | 8.54                       | 6.11-10.97 |         |
| Pleural metastasis   |        |        |                            |            |         |
| Yes                  | 34     | 28     | 6.00                       | 2.94-9.05  | 0.040   |
| No                   | 60     | 44     | 10.70                      | 8.87-12.52 |         |
| Lung metastasis      |        |        |                            |            |         |
| Yes                  | 30     | 20     | 10.14                      | 6.60-13.67 | 0.113   |
| No                   | 64     | 52     | 8.30                       | 5.27-11.32 |         |
| Brain metastasis     |        |        |                            |            |         |
| Yes                  | 18     | 15     | 8.70                       | 2.58-14.81 | 0.890   |
| No                   | 76     | 17     | 9.24                       | 6.55-11.92 |         |
| Bone metastasis      |        |        |                            |            |         |
| Yes                  | 26     | 22     | 10.34                      | 5.32-15.35 | 0.660   |
| No                   | 68     | 50     | 8.54                       | 6.70-10.37 |         |
| Liver metastasis     |        |        |                            |            |         |
| Yes                  | 11     | 10     | 12.00                      | 5.41-18.58 | 0.896   |
| No                   | 83     | 62     | 8.70                       | 6.23-11.16 |         |
| Systemic therapy     |        |        |                            |            |         |
| Yes                  | 79     | 57     | 10.60                      | 8.42-12.78 | <0.001  |
| No                   | 15     | 15     | 4.17                       | 0.88-7.45  |         |
| Radiotherapy         |        |        |                            |            |         |
| Yes                  | 44     | 33     | 10.60                      | 8.82-12.37 | 0.033   |
| No                   | 50     | 39     | 6.57                       | 3.23-9.90  |         |

CI : confidence interval, ECOG : Eastern cooperative oncology group, EGFR : epidermal growth factor receptor, NSCLC : non-small cell lung carcinoma. \*Group A : Universal coverage scheme or Social security scheme, Group B : Government or State Enterprise Officer.

The significant prognostic factors ( $p<0.10$ ) in univariate analysis, including health fund group, ECOG performance status, pleural metastasis, receiving radiotherapy and positive for EGFR mutation were further analyzed in Cox-regression model, with the exception for systemic therapy because the decision to perform a systemic therapy relied on an ECOG performance status of the patients.

In multivariate analysis showed that the ECOG performance status 2-4 ( $p<0.001$ ), no record for ECOG ( $p=0.001$ ) and pleural metastasis ( $p=0.017$ ) were the significantly adverse prognostic factors for survivals (Table 5), but health fund group, receiving radiotherapy and positive for EGFR mutation did not contribute to prognostic potential.

Table 5 Cox regression analysis

| Factors                 |           | HR   | 95% CI     | p-value |
|-------------------------|-----------|------|------------|---------|
| Health fund*            | Group A   | 1.86 | 0.79-4.36  | 0.153   |
|                         | Group B   | 1.00 |            |         |
| ECOG performance status | 0-1       | 1.00 |            |         |
|                         | 2-4       | 3.00 | 1.64-5.47  | <0.001  |
|                         | No record | 3.15 | 1.60-6.20  | 0.001   |
| Pleural metastasis      | No        | 1.00 |            |         |
|                         | Yes       | 1.83 | 1.11-3.01  | 0.017   |
| Radiotherapy            | Yes       | 1.00 |            |         |
|                         | No        | 1.01 | 0.98-1.20  | 0.683   |
| EGFR mutation           | Positive  | 1.00 |            |         |
|                         | Negative  | 4.14 | 0.61-27.85 | 0.144   |
|                         | Unknown   | 2.74 | 0.58-12.85 | 0.200   |

CI : confidence interval, ECOG : Eastern cooperative oncology group, EGFR : epidermal growth factor receptor, HR : hazard ratio.

\*Group A : Universal coverage scheme or Social security scheme, Group B : Government or State Enterprise Officer.

## Discussion

In this study, the overall survival of patients received palliative chemotherapy was a bit fewer than other studies<sup>5-6,17-18</sup> (OS 9.5 vs 10.3-12.6 months), however if we explored survival only in patients with ECOG performance status 0 or 1, the survival in this group was comparable to other studies which enrolled only good performance status of patients with ECOG 0 or 1 (12.67 vs 10.3-12.6 months). The overall response rate of our study was similar to others<sup>5-6</sup> (20.9 vs 15.0-22.0%).

At present, although the standard treatment guideline for advanced non-small cell carcinoma recommends for EGFR mutation and ALK rearrangement testing, in our practical study showed that less than 15 percent of patients were really performed for these. Unfortunately, the cost of targeted therapies in Thailand was really high and only the small number of patients were able to make an access to these therapies as a result a lot of physicians decided not to send for such molecular testing. Previous studies<sup>7-11</sup> showed exactly

that patients with positive EGFR mutation advanced non-small cell lung carcinoma who received EGFR-TKI as first-or second-line could achieve median survival 20-30 months, approximately. In our study, however, the two patients who received EGFR-TKI for first line systemic therapy were not tested for EGFR status before starting the treatments consequently the progression free survivals and the overall survivals were shorter than the pivotal studies. Moreover, five patients whose tumors were positive for EGFR mutation status reached median survival at 22.8 months, which was comparable to the previous studies. Nevertheless, none of these patients received first-line TKI, but two patients with stage IIIB received TKI as maintenance therapy and one received TKI as second-line therapy. Unfortunately, all of these three patients had died finally. The other two positive EGFR mutation patients with stage IV disease still had not received TKI and both of them stayed alive with periodic monitoring for their disease statuses.

In palliative and quality care aspects, this study suggested that there was no systematic approach in caring for patients with advanced cancer in our hospital. For example, only about sixty two percent of the patients were informed about the prognosis of the disease, not all of the patients were appropriately cared for their trouble symptoms such as dyspnea or pain. Studied by Temel and his colleagues<sup>19</sup>, early palliative care in metastatic non-small cell lung carcinoma patients showed not only improvement in quality of life and mood, but also, interestingly, longer survival and less aggressive therapy at the end of life than those who received only standard of care. Therefore, this is an opportunity to improve quality of care in order to provide better care to patients in our institute, like a multidisciplinary care approach and a pre-printed medical record form especially in a palliative care aspect. Most importantly, quality cancer care<sup>20</sup> is rather than palliative or multidisciplinary care, such as providing the patient a chance to get access to clinical trials, providing them an end-of-life care setting, etc. Thus, there is an opportunity to develop our quality cares in our hospital such as a co-operation with a medical school or a private organization to join a clinical study for achieving other innovative therapies.

In multivariate analysis, our study showed that the poor ECOG performance status, no record for ECOG performance status and pleural metastasis were unfavorable prognostic factors for the overall survival. Like other studies<sup>21-23</sup> patients with poor ECOG performance status had shorter survival time. Similarly, in our study, patients with no record for their ECOG performance statuses also had shorter survival time than those who were ECOG performance status 0-1. The no record for patient ECOG performance status is not only

the poor prognostic factor for the over survival, but also an indicator of an incomplete medical record. Our study showed that the pleural metastasis had shorter survival time, but other studies suggested that liver<sup>23-24</sup>, subcutaneous<sup>23</sup>, adrenal<sup>21</sup>, bone<sup>24</sup> metastases were poor prognostic factors for survival in advanced non-small cell lung carcinoma. Although EGFR status was a good prognostic factor showed in many studies<sup>25-26</sup>, but not in others<sup>27-28</sup>. In our study, EGFR status did not contribute to prognostic factor, however, the negative for EGFR mutation had a tendency to have a worse prognosis with HR=4.14, in other words, the positive for EGFR mutation tended to have a better survival. Nevertheless, the small number of the patients were tested for EGFR status as a consequence this caused the limitation to interpret the result.

### Conclusion

Our study revealed that the survival time of advanced non-small cell lung carcinoma of our patients receiving systemic chemotherapy was comparable to other studies. An improvement in the palliative care and other aspects of quality cancer care were necessary for patient care development in our hospital. The poor ECOG performance status, no record for ECOG performance status and having pleural metastasis were poor prognostic factors for the overall survival.

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