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Investigation of the outpatient chemotherapy for lung cancer patients in Tokushima University Hospital

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Abstract : Platinum-doublet regimens and docetaxel as first- and second-line chemotherapy, respectively, are shown to prolong the survival of lung cancer patients in various randomized phase III studies. However, the evidence for the efficacy of chemotherapy for lung cancer in the clinical practice is still insufficient. In the present study, we investigated the effectiveness and safety of outpatient chemotherapy for lung cancer in the clinical practice. Ninety-four lung cancer cases were retrospectively analyzed. Among these cases, 67 (71.3%) were non-small cell lung cancer (NSCLC) and 27 (28.7%) were small cell lung cancer (SCLC). The response rates in SCLC and NSCLC patients were 55.6% (15/27) and 16.9% (11/65), respectively. Objective tumor response rates for the patients were found to decrease substantially with each line of treatment as described previously. All adverse events were well tolerated and no treatment-related death was observed. Median time to treatment failures (TTFs) of first-line treatment were 10.1 months and 4.8 months in SCLC and NSCLC, respectively. These findings indicate that even in the setting of clinical practice, the efficacy and safety of chemotherapy is strictly insured by the appropriate therapeutic management. J. Med. Invest. 58 : 219-226, August, 2011

Keywords **:** *outpatient chemotherapy, lung cancer, best overall response, time to treatment failure*

INTRODUCTION

Lung cancer is the leading cause of cancer mortality in developed countries, and its incidence continues to increase (1). In spite of the improvement in both diagnosis and treatment, the prognosis of patients with advanced lung cancer is still poor (2). Thus, when treating advanced lung cancer patients, it is essential to make an effort to maintain patient's quality of life (QOL) without decreasing the quality of treatment. In this point of view, outpatient chemotherapy has been considered to contribute

Abbreviations : NSCLC : non-small cell lung cancer, SCLC : small cell lung cancer, TTF : time to treatment failure, QOL : quality of life, CTCAE v3.0 : Common Terminology Criteria for Adverse Events version 3.0, CR : complete response, PR : partial response, SD : stable disease, PD : progressive disease, RECIST : Response Evaluation Criteria in Solid Tumors, BOR : best overall response, ECOG : Eastern Cooperative Oncology Group.

Received for publication May 30, 2011 ; accepted July 19, 2011.

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to maintain QOL of cancer patients (3), and in many facilities outpatient chemotherapy has become standard treatment strategy.

The first-line platinum based combination chemotherapy and the second-line chemotherapy with docetaxel are currently recommended as the standard approach for chemotherapy-naïve patients with advanced lung cancer and NSCLC patients who are refractory to the first-line chemotherapy, respectively (4, 5). On the basis of randomized phase III studies, it is clearly shown that these therapeutic strategies prolong the survival and that improve patient's QOL by controlling disease-related symptoms (6). However, these evidences were usually obtained from non-elderly patients with good performance status. In the clinical setting, we often encounter advanced lung cancer patients in the elderly and/or with declined performance status, who are not eligible for usual eligibility criteria of randomized phase III studies. For these patients, we can hardly indicate the standard chemotherapeutic regimens and no established alternative regimens are demonstrated. Therefore, it seems important to understand the current status of chemotherapy for lung cancer in the settings of clinical practice. In this report, we focused on outpatient chemotherapy which has been done in our department and retrospectively analyzed the efficacy of the treatments, frequency of adverse events as well as QOL of the patients.

PATIENTS AND METHODS

Patients

The retrospective analysis was conducted using data from patients who had diagnosed as lung cancer in the Department of Respiratory Medicine and Rheumatology in Tokushima University Hospital. Examination of patient records from January 2007 to August 2008, revealed that 94 cases were found to fit the eligibility criteria (Different chemotherapy regimens in one patient were analyzed as separate cases).

Eligibility Criteria

Patients were required to have histological or cytological confirmation of lung cancer ; life expectancy > 12 weeks ; adequate bone marrow, hepatic and renal function ; with the presence of at least one measurable indicator lesion assessed by conventional computed tomography scan. The patients who received at least one chemotherapeutic regimen in outpatient chemotherapy unit in Tokushima University Hospital were enrolled in this study. The patients had to give written informed consent for receiving outpatient chemotherapy.

Chemotherapy

For the treatment, clinically approved anti-cancer drugs were used. Generally, patients were admitted to the hospital to receive first cycle of the treatment. After confirming the level of adverse events, following treatment was performed at the outpatient clinic. All adverse events were graded according to Common Terminology Criteria for Adverse Events version 3.0 (CTCAE v3.0) (7). When grade 4 hematologic toxicities and/or grade 3 or worse non-hematologic toxicities were occurred, the dosage of the drug was reduced to 80% of original dose. The use of molecular-targeted agents such as epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) was not investigated in this study.

Objective Tumor Response, Time to Treatment Failure, Quality of Life

Response was determined in comparison with baseline assessment of measurable disease or evaluable disease and confirmed 4 weeks later. Objective tumor responses were defined as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD), using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.0 (8). Best overall response (BOR) was defined as the best objective response during chemotherapy. TTF was calculated from the date of the initiation of treatment up to the date of failure (defined as progression, relapse, death, withdrawal due to adverse events, patient's refusal, loss to follow-up or start of new anticancer therapy) (9).

Statistical Analysis

Survival curves were estimated by the Kaplan-Meier method. The log-rank test was used to compare patient's survival between groups. $p < 0.05$ was considered to be statistically significant.

RESULTS

Data have been obtained retrospectively for 94 out of more than 100 cases with lung cancer. The characteristics of the patients are shown in Table 1. Among 94 cases, there were 81 (86.2%) men and 13

Table 1. Patient characteristics

No. cases	94
Male/Female	81/13
Age (Years)	
Median (Range)	67 (36-86)
ECOG Performance Status	
0	12 (12.8%)
1	69 (73.4%)
2	13 (13.8%)
Stage	
IIB	4 (4.3%)
IIIA	4 (4.3%)
IIIB	17 (18.1%)
IV	69 (73.4%)
Histology	
NSCLC	
Adenocarcinoma	38 (40.4%)
Squamous cell carcinoma	20 (21.3%)
Large cell carcinoma	5 (5.3%)
Unknown	4 (4.3%)
SCLC	27 (28.7%)

(13.8%) women with mean age of 67 years (range : 36-86 years old). Sixty-nine (73.4%) cases had stage IV lung cancer and 81 (86.2%) had Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. In terms of histological background, 67 (71.3%) cases were NSCLC and 27 (28.7%) were SCLC. Among NSCLC, adenocarcinoma was the most commonly seen, followed by squamous cell carcinoma, large cell carcinoma. Compared to the previous report (10), the frequency of adenocarcinoma was lower and that of small cell lung cancer was higher in this study.

The different chemotherapy regimens received by these patients for each line treatment are shown in Table 2. Patients had received platinum-based therapy as first-line (94.3%) or second-line (43.3%) treatment. Twenty-four out of 27 cases (88.9%) with SCLC were treated with platinum-based therapy irrespective of treatment line. In NSCLC, 21 out of 23 patients (91.3%) received platinum-based therapy

Table 2A. Chemotherapy regimens for small cell lung cancer

Regimen	treatment line				total
	1st (n=12)	2nd (n=10)	3rd (n=2)	4th or more (n=3)	
Platinum-based (%)	12 (100.0)	9 (90.0)	1 (50.0)	2 (66.7)	
CBDCA+CPT-11	8	6	1	2	17
CBDCA+VP-16	2	2			4
CDDP+CPT-11	2	1			3
Others (%)	0 (0.0)	1 (10.0)	1 (50.0)	1 (33.3)	
AMR		1	1	1	3
total	12	10	2	3	27

Table 2B. Chemotherapy regimens for non-small cell lung cancer

Regimen	treatment line				total
	1st (n=23)	2nd (n=20)	3rd (n=12)	4th or more (n=12)	
Platinum-based (%)	21 (91.3)	4 (20.0)	0 (0.0)	0 (0.0)	
CBDCA+VNR	8	1			9
CBDCA+PTX	5	1			6
CDDP+VNR	3	1			4
CBDCA+GEM	2	1			3
CBDCA+DTX	2				2
CDDP+GEM	1				1
Others (%)	2 (8.7)	16 (80.0)	12 (100.0)	12 (100.0)	
VNR	1	2			3
CPT-11	1			3	4
DTX		8	9	3	20
GEM+VNR		5	1		6
GEM		1	2	5	8
AMR				1	1
total	23	20	12	12	67

CBDCA : Carboplatin, CPT-11 : Irinotecan, VNR : Vinorelbine, PTX : Paclitaxel, CDDP : Cisplatin, VP-16 : Etoposide, GEM : Gemcitabine, DTX : Docetaxel, AMR : Amrubicin

as first-line chemotherapy, while as second-line chemotherapy, 16 patients (80.0%) were treated with single or combination of non-platinum agents. The regimens for third or more lines of treatment varied widely.

Among 94 cases, 92 were eligible for the evaluation of objective tumor response assessed by RECIST version 1.0. As shown in Table 3, 2 CR and 24 PR were observed in the 92 assessable cases for overall response rate was 28.3%. The response rates in SCLC and NSCLC patients were 55.6% (15/27) and 16.9% (11/65), respectively. The overall disease control rate (response plus SD) was 94.6% (87/92), indicating the diseases of almost all patients were controlled by the chemotherapy at least 2 months. We next evaluated the response rates for each line of treatment. Objective tumor response rates for the patients were found to decrease substantially with each line of treatment (Fig. 1). The response rates of the first, second, third and fourth or more lines of treatment for SCLC and NSCLC were 83.3% and 38.1%, 50.0% and 15.0%, 0% and 0%, 0% and 0%, respectively.

Grade 3-4 adverse events of chemotherapy, assessed by CTCAE v3.0, are shown in Table 4. The frequencies of grade 3-4 toxicities observed in the present study were comparable with the previous reports (11, 12). The most common grade 3-4 toxicities were leukopenia and neutropenia, which were seen in 18 (19.1%) and 22 (23.4%) of lung cancer patients, respectively. All adverse events were well

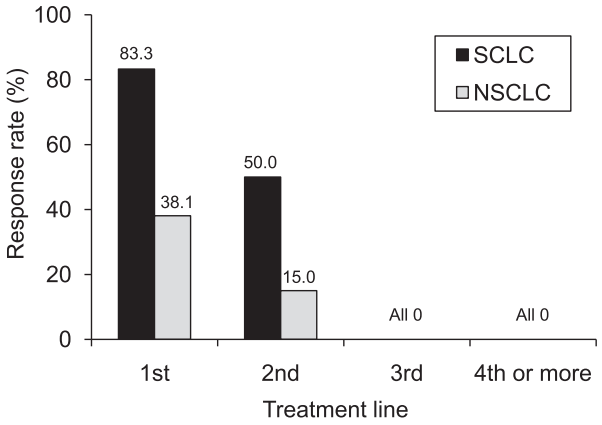

Figure 1 Response rates for each line of chemotherapy in SCLC and NSCLC patients.

Table 4. Common Terminology Criteria for Adverse Events version 3.0 grade 3-4 toxicity.

Adverse events	Number of patients (%)		
	G3	G4	G3+G4
Hematological toxicities			
Leukopenia	17 (18.1)	1 (1.1)	18 (19.1)
Neutropenia	11 (11.7)	11 (11.7)	22 (23.4)
Anemia	6 (6.4)	1 (1.1)	7 (7.4)
Thrombocytepenia	3 (3.2)	0 (0.0)	3 (3.2)
Hyponatremia	1 (1.1)	0 (0.0)	1 (1.1)
Non-hematological toxicities			
Infection	6 (6.4)	0 (0.0)	6 (6.4)
Pulmonary disorder	3 (3.2)	0 (0.0)	3 (3.2)
Anorexia	1 (1.1)	0 (0.0)	1 (1.1)
Diarrhea	1 (1.1)	0 (0.0)	1 (1.1)

Table 3A. Best overall response (BOR) in each line of chemotherapy for small cell lung cancer.

BOR	treatment line				total (%)
	1st (n=12)	2nd (n=10)	3rd (n=2)	4th or more (n=3)	
Complete response	1				1 (3.7)
Partial response	9	5			14 (51.9)
Stable disease	2	5	2		9 (33.3)
Progressive disease				3	3 (11.1)
Not evaluable					0 (0.0)
total	12	10	2	3	27

Table 3B. Best overall response (BOR) in each line of chemotherapy for non-small cell lung cancer.

BOR	treatment line				total (%)
	1st (n=23)	2nd (n=20)	3rd (n=12)	4th or more (n=12)	
Complete response	1				1 (1.5)
Partial response	7	3			10 (14.9)
Stable disease	13	17	11	11	52 (77.6)
Progressive disease			1	1	2 (3.0)
Not evaluable	2				2 (3.0)
total	23	20	12	12	67

tolerated and no grade 5 toxicities were seen in the present study. The reasons of emergency admission throughout chemotherapy are shown in Table 5. Fifteen out of 94 cases were forced unscheduled admission to our hospital. Infectious diseases, such as pneumonia, in accordance with neutropenia were prominent. The rate of emergency admission during chemotherapy was 16.0%, which was comparable with the report that 20.8% of cases required hospital admission during outpatient chemotherapy (13).

Finally, we examined the TTFs of first-line and second or more lines of chemotherapy (Fig. 2). In SCLC, median TTFs of first-line and second or more lines of treatment were 304 days (10.1 months) and 145 days (4.8 months), respectively. In NSCLC, median TTFs of first-line and second or more lines of treatment were 188 days (6.3 months) and 132 days (4.4 months), respectively. Median TTFs of first-line chemotherapy tended to be longer than that of second or more lines in both SCLC and NSCLC, but not significant (p=0.1620 and 0.3650, respectively). The median TTFs observed in the present study were comparable with previously reported results (14), strongly indicating that the efficacy of chemotherapy might be retained by the appropriate therapeutic management even in the setting of clinical practice, such as outpatient chemotherapy unit.

Table 5. The reason of emergency admission during chemotherapy.

Events	No. of patients (%)
Pneumonia	5 (5.3)
Pulmonary disorder	3 (3.2)
Infection	2 (2.1)
Anorexia	1 (1.1)
Hemosputum	1 (1.1)
Numbness in extremities	1 (1.1)
Pain	1 (1.1)
Terminal care	1 (1.1)
Total	15 (16.0)

DISCUSSION

In the present study, we investigated the current status of outpatient chemotherapy for lung cancer. Even in the setting of clinical practice, the efficacy, which was assessed by the response rate and the TTF, and the safety of chemotherapeutic agents were demonstrated to be comparable with the previously reported results in randomized phase III studies.

Platinum-doublet regimens combining cisplatin or carboplatin with etoposide, irinotecan are extensively administered for the first-line chemotherapy in SCLC. In a multicenter, randomized, phase III study to compare irinotecan plus cisplatin with etoposide plus cisplatin in patients with extensive SCLC, the response rates and the progression-free survivals were reported to be 67.5-84.4% and 4.8-6.9 months, respectively (11). For advanced NSCLC patients, combination chemotherapy, usually platinum-based, is also currently the first-line therapy of choice (15). Based on various studies, doublet regimens combining cisplatin or carboplatin with paclitaxel, gemcitabine, docetaxel, vinorelbine or irinotecan are chosen. Various studies have shown similar degrees of efficacy among different combinations in

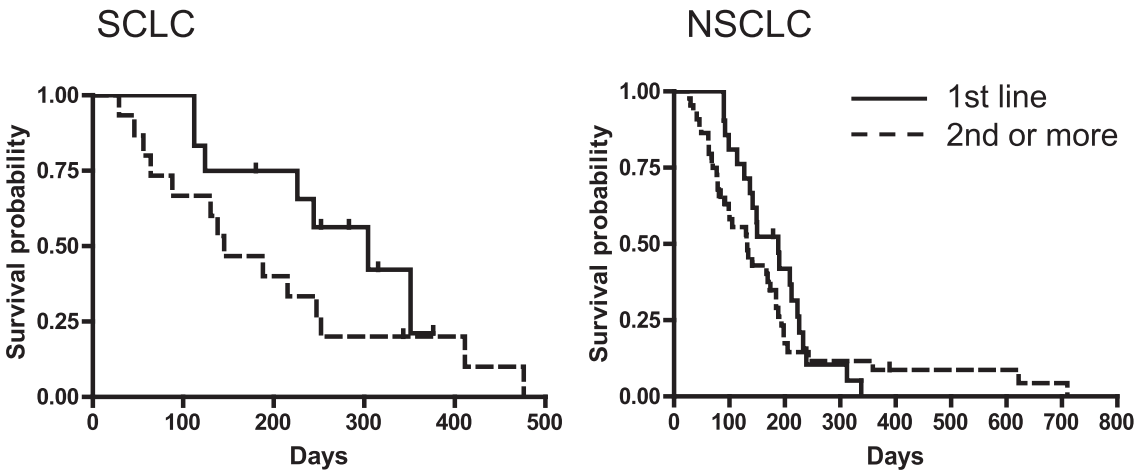

Figure 2 Kaplan-Meier curve showing time to treatment failure of SCLC and NSCLC patients who received 1st or 2nd or more chemotherapy.

the treatment of advanced NSCLC. For instance, in a randomized phase III trial including over 100 patients in each study group, cisplatin plus irinotecan was compared with cisplatin or carboplatin plus paclitaxel, gemcitabine or vinorelbine. No significant differences were reported in terms of the efficacy of these four chemotherapeutic regimens ; in each arm, the response rates were 30.1-33.1%, and the median TTFs were 3.0-3.3 months (14). In the present study, the clinical efficacy of the first-line chemotherapy for SCLC and NSCLC patients were comparable with previously reported results ; in each group, the response rates were 83.3% and 38.1% (Table 3), the median TTFs were 10.1 months and 6.3 months (Fig. 2), respectively. These results indicate that the efficacy of chemotherapy might be retained by the appropriate therapeutic management even in the setting of clinical practice, such as outpatient chemotherapy unit.

The objective tumor response rates and the median overall survival time for lung cancer are well known to decrease substantially with each line of chemotherapy. The response rates and the median overall survival time of the first, second, third and fourth lines of treatment for advanced NSCLC were reported to be 20.9% and 15.7 months, 16.3% and 9.8 months, 2.3% and 5.4 months, 0% and 5.9 months, respectively (16). In the present study, the response rates of the first, second, third or more lines of treatment for NSCLC were 38.1%, 15.0%, and 0%, respectively (Table 3, Fig. 1), in consistent with previous reports.

When treating patients with cancer, physicians usually seek the best therapeutic results. However, patients do not always have exactly the same priorities when setting therapeutic goals. Generally, patients wish to experience symptom improvement, few toxic effects and better quality of life, in addition to expect to live longer. A study conducted by Silvestri *et al*, which enrolled 81 patients with advanced NSCLC already treated with chemotherapy, showed that many patients would choose chemotherapy treatment for its effects on quality of life rather than for the potential survival offered by the treatment (17). Only 25% would choose chemotherapy if benefits were exclusively related to survival. More recently, it was noted that nearly 75% of patients would choose the therapeutic regimen according to the related adverse effects (18). Thus, because advanced lung cancer is unlikely to be cured, we always must take the risk of adverse effects into account when introducing chemotherapy, especially in outpatient clinic-based treatment.

In the present study, 19.1%, 23.4%, 7.4% and 3.2% of lung cancer patients developed grade 3 or worse leukopenia, neutropenia, anemia and thrombocytopenia, respectively. Grade 3 or worse infections including bacterial pneumonia, pulmonary disorders, diarrhea and anorexia occurred in 6.4%, 3.2%, 1.1% and 1.1%, respectively, of lung cancer patients. The incidence of hematologic and non-hematologic toxicities was comparable with the previously reported results in randomized phase III studies (14). All adverse events were well tolerated and no grade 5 toxicities were developed in the present study. Moreover, the rate of emergency admission during chemotherapy was 16.0%, which was comparable with the report that 20.8% of cases required hospital admission during outpatient chemotherapy (13). Taken these results into consideration, the safety of treatment is insured and QOL of the patients with lung cancer seems to be well maintained during treatment in outpatient chemotherapy unit in our hospital.

Several lines of evidence indicate the effectiveness of multidisciplinary team for the management of lung cancer. Coory *et al* have demonstrated that the intervention of multidisciplinary team leads to an increase in the percentage of patients undergoing surgical resection or an increase in the percentage of patients undergoing chemotherapy or radiotherapy with curative intent (19). Moreover, it seems intuitively obvious that multidisciplinary teams should improve outcomes for lung cancer patients, while currently available evidence is limited. In our institution, we are scheduled to launch multidisciplinary team, including certified nurses and pharmacists, to discuss the diagnosis and management of patients with lung cancer.

In conclusion, we investigated the current status of chemotherapy for lung cancer in outpatient chemotherapy unit in Tokushima University Hospital. Even in the setting of clinical practice, the efficacy and safety of chemotherapy was demonstrated is strictly insured by the appropriate therapeutic management.

ACKNOWLEDGEMENTS

We thank the members of the Department of Respiratory Medicine and Rheumatology and Department of Medical Oncology, the University of Tokushima for the fruitful discussion. We also thank

the staffs of outpatient clinic in Tokushima University Hospital for the cooperation in outpatient chemotherapy.

REFERENCES

1. Greenlee RT, Murray T, Bolden S, Wingo PA : Cancer statisitics, 2000. CA Cancer J Clin 50 : 7-30, 2000
2. Bunn PA Jr, Thatcher N : Systemic treatment for advanced (stage IIIb/IV) non-small cell lung cancer : more treatment options ; more things to consider. Conclusion. Oncologist 13(Suppl 1) : 37-46, 2008
3. Scalamonga R, Brugnatelli S, Tinelli C, Sagrada P, Gattoni E, Tronconi MC, Riccardi A, Luchena G, Corazza GR : UFT as maintenance therapy in patients with advanced colorectal cancer responsive to the FOLFOX4 regimen. Oncology 72 (5-6) : 267-273, 2008
4. Schiller JH, Harrington D, Belani CP, Langer C, Sandler A, Krook J, Zhu J, Johnson DH ; Eastern Cooperative Oncology Group : Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. N Engl J Med 346 : 92-98, 2002
5. Lynch TJ Jr : Review of two phase III randomized trials of single-agent docetaxel in previously treated advanced non-small cell lung cancer. Semin Oncol 28(Suppl 9) : 5-9, 2001
6. Thatcher N : First- and second-line treatment of advanced metastatic non-small-cell lung cancer : a global view. BMC Proc 2(Suppl 2) : S3-S8, 2008
7. Trotti A, Colevas AD, Setser A, Rusch V, Jaques D, Budach V, Langer C, Murphy B, Cumberlin R, Coleman CN, Rubin P : CTCAE v3.0 : development of a comprehensive grading system for the adverse effects of cancer treatment. Semin Radiat Oncol 13 : 176-181, 2003
8. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, Verweij J, Van Glabbeke M, van Oosterom AT, Christian MC, Gwyther SG. : New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst 92 : 205-216, 2000
9. Tan EH, Rolski J, Grodzki T, Schneider CP, Gatzemeier U, Zatloukal P, Aitini E, Carteni G, Riska H, Tsai YH, Abratt R : Global Lung Oncology Branch trial 3 (GLOB3) : final results of a randomised multinational phase III study alternating oral and i.v. vinorelbine plus cisplatin versus docetaxel plus cisplatin as first-line treatment of advanced non-small-cell lung cancer. Ann Oncol 20(7) : 1249-1256, 2009
10. Travis WD : Histological typing of lung cancer and pleural tumours. WHO International Histological Classification of Tumours. 3rd ed., Springer, Berlin, 1999
11. Noda K, Nishiwaki Y, Kawahara M, Negoro S, Sugiura T, Yokoyama A, Fukuoka M, Mori K, Watanabe K, Tamura T, Yamamoto S, Saijo N ; Japan Clinical Oncology Group : Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small-cell lung cancer. N Engl J Med 346 : 85-91, 2002
12. Park JO, Kim SW, Ahn JS, Suh C, Lee JS, Jang JS, Cho EK, Yang SH, Choi JH, Heo DS, Park SY, Shin SW, Ahn MJ, Lee JS, Yun YH, Lee JW, Park K : Phase III trial of two versus four additional cycles in patients who are non-progressive after two cycles of platinum-based chemotherapy in non small-cell lung cancer. J Clin Oncol 25 : 5233-5239, 2007
13. Majem M, Galán M, Pérez FJ, Muñoz M, Chicote S, Soler G, Navarro M, Martínez-Villacampa M, García del Muro X, Dotor E, Laquente B, Germà JR : The oncology acute toxicity unit (OATU) : an outpatient facility for improving the management of chemotherapy toxicity. Clin Transl Oncol 9 : 784-788, 2007
14. Ohe Y, Ohashi Y, Kubota K, Tamura T, Nakagawa K, Negoro S, Nishiwaki Y, Saijo N, Ariyoshi Y, Fukuoka M : Randomized phase III study of cisplatin plus irinotecan versus carboplatin plus paclitaxel, cisplatin plus gemcitabine, and cisplatin plus vinorelbine for advanced non-small-cell lung cancer : Four-Arm Cooperative Study in Japan. Ann Oncol 18 : 317-323, 2007
15. Ramalingam S, Belani C : Systemic chemotherapy for advanced non-small cell lung cancer : recent advances and future directions. Oncologist 13(Suppl 1) : 5-13, 2008
16. Massarelli E, Andre F, Liu DD, Lee JJ, Wolf M, Fandi A, Ochs J, Le Chevalier T, Fossella F, Herbst RS : A retrospective analysis of the outcome of patients who have received two prior chemotherapy regimens including platinum and docetaxel for recurrent non-small-cell lung

cancer. Lung Cancer 39 : 55-61, 2003
17. Silvestri G, Pritchard R, Welch HG. : Preferences for chemotherapy in patients with advanced non-small cell lung cancer : descriptive study based on scripted interviews. BMJ 317 : 771-775, 1998
18. Dubey S, Brown RL, Esmond SL, Bowers BJ, Healy JM, Schiller JH : Patient preferences in choosing chemotherapy regimens for advanced non-small cell lung cancer. J Support Oncol 3 : 149-154, 2005
19. Coory M, Gkolia P, Yang IA, Bowman RV, Fong KM : Systematic review of multidisciplinary teams in the management of lung cancer. Lung Cancer 60 : 14-21, 2008