博 士 學 位 論 文

Survival Outcomes in Patients with Advanced-Stage IIIb/Ⅳ Non-Small Cell Lung Cancer Treated with *HangAm-Plus*

항암플러스로 치료받은 IIIb/Ⅳ기
진행성 비소세포성폐암 환자의 생존율 분석

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2012年 2月

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이 論文을 韓醫學博士學位
請求論文으로 提出함

2011年 10月

大 田 大 學 校 大 學 院
韓醫學科 韓方內科學專攻

房 善 輝

房 善 輝의 韓醫學 博士學位

請求論文을 認准함

2011年 12月

學 位 論 文 審 査 委 員 會

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Ⅰ. Introduction

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries[1]. The burden of cancer is increasing in economically developing countries as a result of population aging and growth as well as, increasingly, an adoption of cancer-associated lifestyle choices including smoking, physical inactivity, and 'westernized' diets.

Lung cancer has been the most common cancer in the world for several decades, and by 2008, there were an estimated 1.61 million new cases, representing 12.7% of all new cancers. It was also the most common cause of death from cancer, with 1.38 million deaths (18.2% of the total)[2]. According to 2008 statistics from Korean National Cancer Center, lung cancer was ranked fourth (10.5%) highest in cancer incidence in Korea. Especially in male population, lung cancer was ranked 3rd (14.4%) followed by stomach cancer (20.3%) and colorectal cancer (14.6%)[3]. In 2009 cancer mortality, lung cancer ranked 1st place (21.4%) in Korea[4]. Moreover, in 2009 cancer statistics of the United States, lung cancer ranked 1st place for both incidence (14.8%) and mortality (28.3%) rate[5]. Markedly, mortality rate is relatively higher than that of incidence which makes lung cancer one of the most intractable cancers. Generally, lung cancer is divided into two histological subgroups: non-small cell and small cell. It is important to distinguish non-small cell lung cancer (NSCLC) from small cell lung cancer (SCLC) because the two types are usually treated differently[6]. NSCLC accounts for approximately 85% of all cases of lung cancer[7]. NSCLC consists of three major cell types; adenocarcinoma, squamous cell carcinoma, and large cell carcinoma[8]. The treatment of NSCLC is determined by disease stage. Surgery continues to be the mainstay treatment for early-stage and localized disease. Multimodal therapy has become the norm for regionally advanced disease. However, stage IIIb or IV NSCLC patients are

candidates for palliative chemotherapy[9].

HangAm-Plus (HAP) has been used to treat solid tumors such as lung, pancreatic, colorectal, and stomach cancers at the East West Cancer Center (EWCC) Dunsan Oriental Hospital (Daejeon South Korea) since its development in 1996[10-15]. Several research findings have supported the therapeutic role of HAP in immune function, anti angiogenesis, and inhibition of cancer cell proliferation and metastasis[10-15]. Case reports have even been selected as part of the National Cancer Institute's Best Case Series Program using HAP[19].

Yoo et. al reported a case of 7-year follow-up about recurred squamous cell lung carcinoma treated with HAP. Park et. al performed a retrospective cohort analysis for lung cancer patients treated with HAP[20]. Moreover, Jeong et. al carried out a prospective study on inoperable NSCLC treated with HAP[21]. These previous studies have already reported therapeutic effects of HAP in NSCLC patients[22]. The goal of this study is to evaluate the efficacy of HAP as a second-line over treatment of advanced-stage IIIb/Ⅳ NSCLC.

Ⅱ. Materials and Methods

2.1. Patients

Six NSCLC patients participated in this study from April 2010 to October 2011 at the EWCC. The treatment plan was explained and informed consent was obtained from the patients. Eligibility criteria included the following:

(1) Patients with cytologically or histologically verified NSCLC stage IIIB or IV who were not candidates for treatment with a curative intent;
(2) Stage IIIb/IV NSCLC patients who refused first-line chemotherapy or failed at least one cycle of chemotherapy;
(3) Patient with measurable malignant lesion using the international standard of Response Evaluation Criteria in Solid Tumors (RECIST)[23]; complete/partial response (CR/PR), progression/stable disease (PD/SD);
(4) Eastern Cooperative Oncology Group (ECOG)[24] score ≤ 2;
(5) Patients with expected survival of at least 3 months;
(4) Completion of anticancer drugs and/or radiation treatment 3 weeks prior to participation;
(5) Recovery from all adverse effects of anticancer drugs and/or radiation treatment;
(6) Proper bone marrow function (peripheral absolute granulocyte count > 150 × 10^9/L, platelet count > 100 × 10^9/L);
(7) Proper liver function (bilirubin ≤ 1.5 mg/dL, serum glutamic pyruvic transaminase or serum glutamic oxaloacetic transaminase < 3 × normal) and kidney function (creatinine ≤ 1.5 mg/dL).

2.2. Baseline

Demographic and clinical data (age, gender, histological or cytological tumor type, performance status, disease stage, body height and weight) as well as laboratory measures (hemoglobin, leukocyte and platelet counts, sodium, potassium, calcium, albumin, spartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, alkaline phosphatase, lactate dehydrogenase and creatinine) were recorded.

2.3. Treatment

HAP is the name of an anti cancer herbal drug which is using in EWCC for the past decades. HAP consists of 8 herbs (Table 1). HAP is usually taken three times a day (TID), 1,000 or 2,000 mg at a time, after meals (total 3,000 or 6,000 mg/day).

Table 1. Ingredients of HangAm-Plus

Scientific name	Relative amount (mg)
Panax noto-ginseng (Burk.) f.H. Chen	84.0
Cordyceps militaris (Berk.) Sacc.	64.0
Tulipa edulis Bak.	64.0
Panax ginseng C. A. Mey.	64.0
Bos taurus domesticus Gmelin	64.0
Pinctada martensii Dunker	64.0
Boswellia carterii Birdw.	48.0
Commiphora molmol Engl.	48.0
Total amount (1 capsule)	500.0

2.4. Assessment of disease progression

Tumor response rate was measured with computed tomography (CT) scan. CT scan of the patients were taken at initial administration of HAP and after 12 weeks of treatment. Tumor size was recorded using RECIST guidelines[23]. Compared with initial tumor size, disappearance of all target lesions was confirmed as complete response (CR), at least a 30% decrease in the sum of diameters of target lesions was confirmed as partial response (PR), at least a 20% increase in the sum of diameters of target lesions was confirmed as progressive disease (PD), and neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD was confirmed as stable disease (SD).

2.5. Endpoints

Two endpoints were set to evaluate the result:

(1) Survival rate, including overall survival (from initial administration of HAP to death or last follow-up time) and progression-free survival (the time from randomization to the first of either recurrence or relapse, second cancer, or death)[25].

(2) Response rate, measured by the International standard provided by RECIST as complete response, partial response, progressive disease and stable disease[23].

(3) Adverse effects based on Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 during HAP treatment were also investigated[26].

2.6. Statistical analysis

Association between the variables "tumor response", "treatment period" and "survival time" were tested using the fisher's exact tests. Estimations of the median of both overall survival (OS) time and progression free survival (PFS) time have been done using Kaplan Meier analysis based on all the 6 patients. Also the estimates for each group formed by "SD - PD" and "before - after" were obtained

in the same way. The comparisons of group survival functions were done using the log rank tests based on both overall survival time and progression free survival time.

Ⅲ. Results

3.1. Patients characteristics

Characteristics of patients are shown in Table 2. Subjects in this study consisted of two males (33.3%) and four female (66.7%). All six NSCLC patients were histologically diagnosed as adenocarcinoma. Mean age was 61 years. One patient was stage IIIb (16.7%) and 5 patients were stage IV (83.3%).

During the course of the treatment, two patients were treated for less than 100 days (33.3%) and four patients were treated more than 100 days (66.7%). The median duration of HAP treatment was 5.3 month. In the 12-weeks-interval chest CT assessment, three patients had Stable Disease (SD) and other three patients had Progressive Disease (PD) (Table 2, 3).

Table 2. Patients Characteristics

Gender	Male	2 (33.3%)
	Female	4 (66.7%)
Age	Median	61 (47~74)
Biopsy	Adenocarcinoma	6 (100%)
Stage	ⅢIb	1 (16.7%)
	Ⅳ	5 (83.3%)
ECOG*	1	1 (16.7%)
	2	5 (83.3%)
Prior Therapy	Yes	5 (83.3%)
	No	1 (16.7%)
Treatment Duration (Day)	<100	2 (33.3%)
	≥100	2 (33.3%)

*ECOG : Easten Cooperative Oncology Group

Table 3. Patients Summaries

No.	Age	Sex	Stage	ECOG	Treatment Period	RECIST	PFS days	OS days	Remarks (Oct.31 2011)
1	52	M	ⅢIb	2	90	SD	210	398	Expired
2	74	M	Ⅳ	2	81	SD	512	512	Alive
3	74	F	Ⅳ	2	407	PD	88	497	Alive
4	47	F	Ⅳ	1	170	SD	497	497	Alive
5	68	F	Ⅳ	2	111	PD	94	276	Expired
6	51	F	Ⅳ	2	103	PD	97	234	Expired

ECOG = Eastern Cooperative Oncology Group (0 = fully active; 1 = restricted in physically strenuous activity; 2 = up and about more than 50% of waking hours; 3 = limited self-care confined to bed or chair more than 50% of waking hours; 4 = totally confined to bed or chair; 5 = dead); RECIST = Response Evaluation Criteria In Solid Tumors(Complete Response (CR) = Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. Partial Response (PR) = At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Progressive Disease (PD) = At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Stable Disease (SD) = Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study) PFS = progression free survival; OS = overall survival.

3.2. Overall survival (OS)

Of the six participating patients, three patients expired during the study period. OS ranged from 234 to 512 days with median survival of 397 days and one year survival rate of 66.7%. Three remaining patients survived as of October 31, 2011. Two in three patients with SD currently are alive and one in three patients with PD expired.

Patients with SD showed longer overall survival than patients with PD in Figure 2. One in two patients under 100 day of HAP administration currently is alive. Two in four patients over 100 day of HAP administration currently is alive. No significant OS variation correlated with administration period in Figure 3.

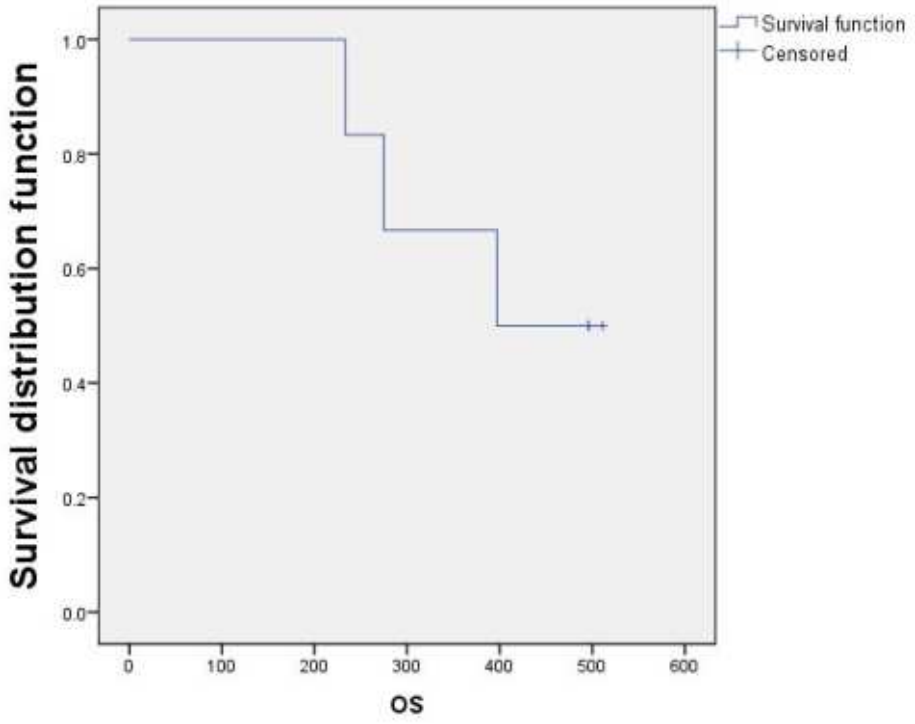

Figure 1. Overall patients survival rate. A total of six patients participated. One year survival rate was 66.7% (SE = 19.2) and median survival time was 397 days with one year survival rate of 66.7%.

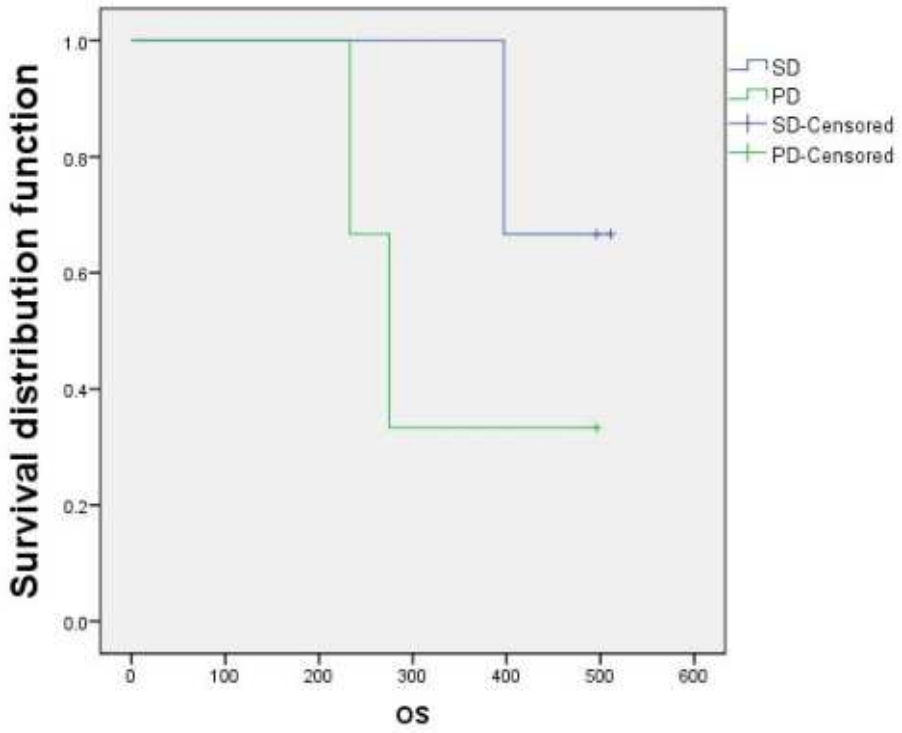

Figure 2. Overall survival rates for tumor response A total of six patients were participated. One patient out of three with Stable Disease (SD) expired and two patients out of three with Progression Disease (PD) expired.

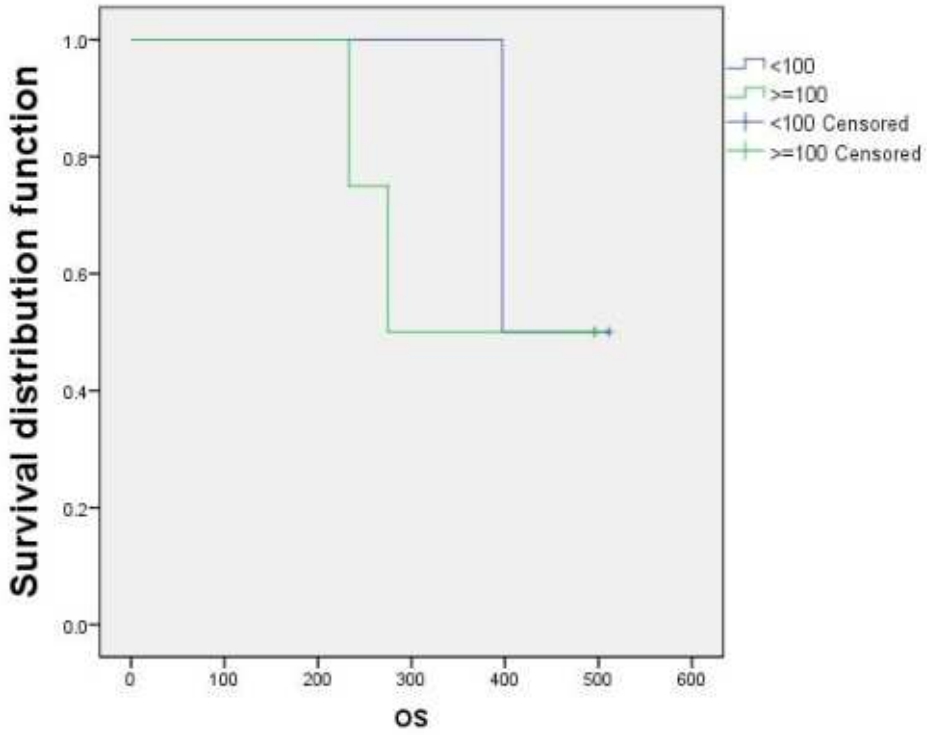

Figure 3. Overall survival rates for treatment period A total of six patients participated. One patient out of two with less than 100 days treatment period were expired and two patients out of four with more than 100 days treatment period were expired.

3.3. Progression-free survival (PFS)

PFS is defined as the time from randomization to the first of either recurrence or relapse, second cancer, or death[25]. PFS of patients ranged from 88 to 512 days and median PFS is 96 days in Figure 4. Patients with SD showed longer PFS period than patients with PD in Figure 5. One in two patients under 100 days of HAP administration had progressed. Three in four patients over 100 days of HAP administration had progressed. There is no significant PFS variation according to administration period in Figure 6.

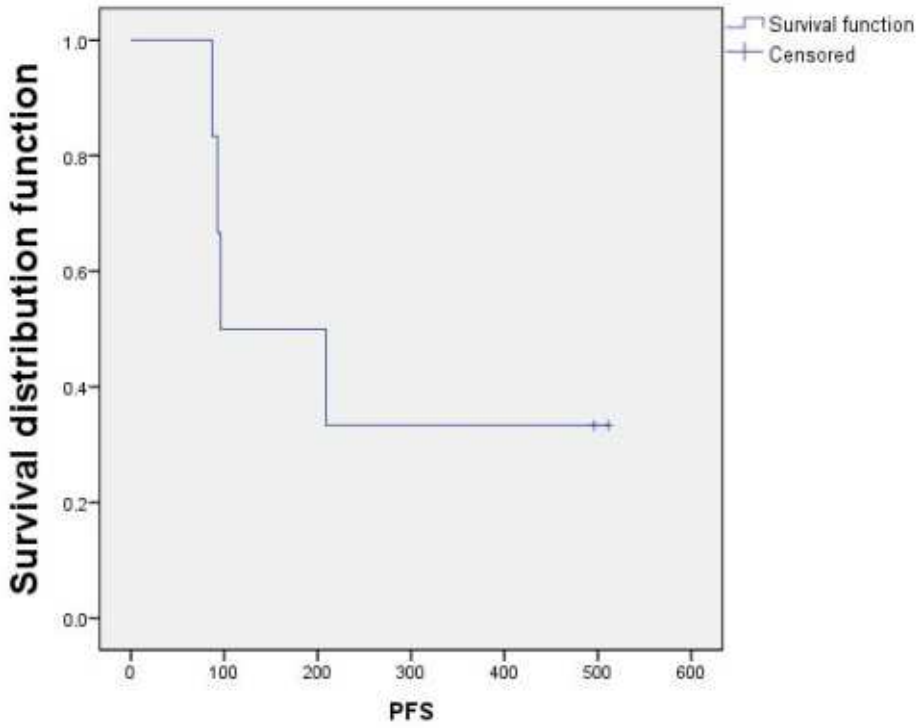

Figure 4. Progression free survival rate A total of six patients participated. Median progression free survival time was 96 days

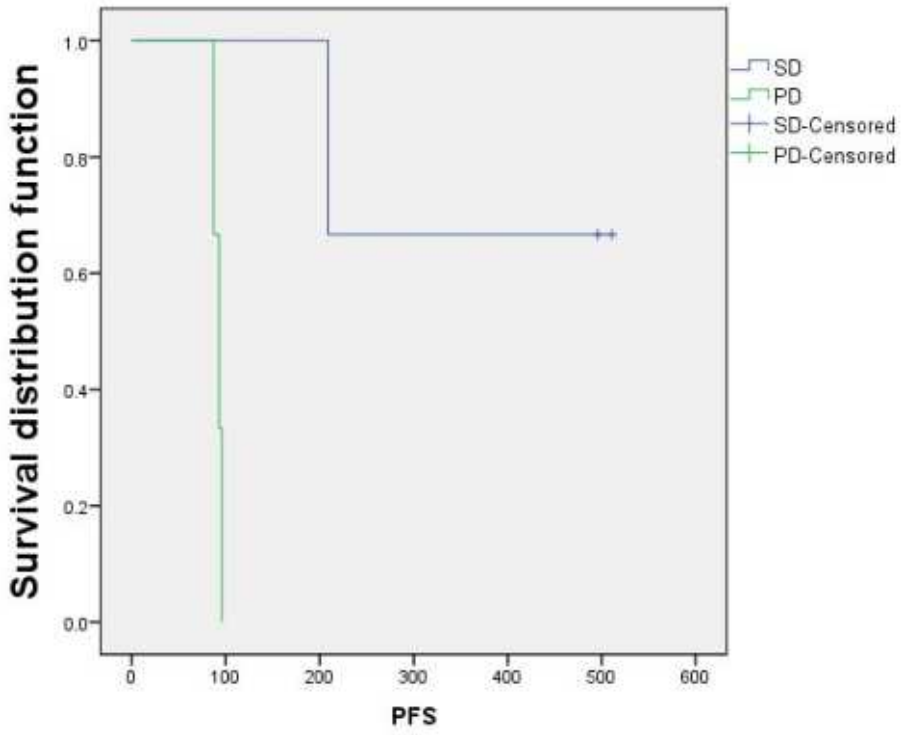

Figure 5. Progression free survival rates for tumor response A total of six patients participated. One patient out of three with SD progressed after within 100 days and all three patients with PD progressed within 100 days.

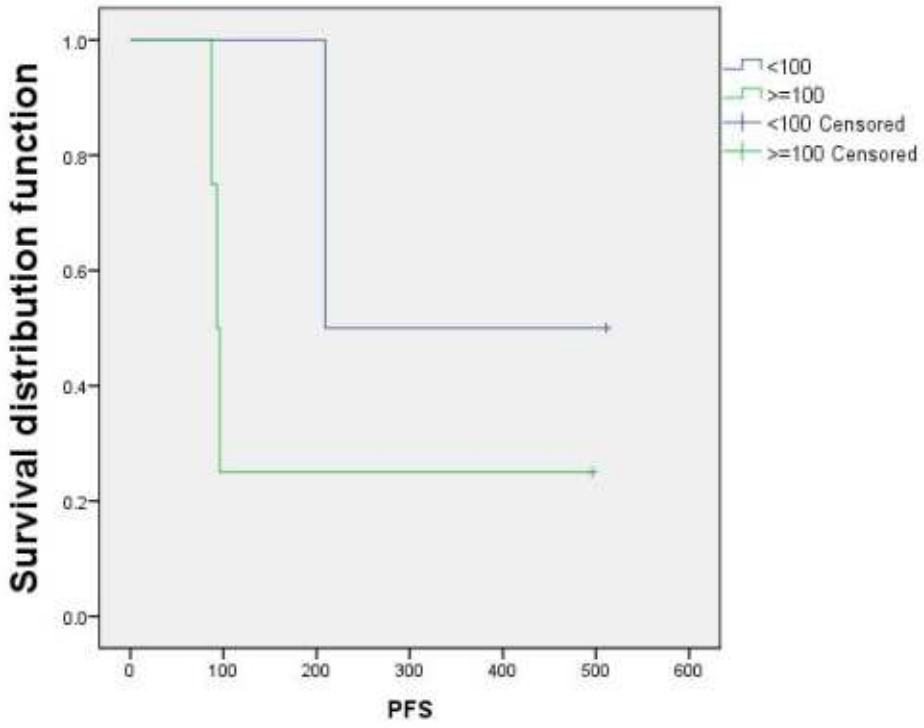

Figure 6. Progression free survival rates for treatment period A total of six patients participated. One patient out of two with less than 100 day treatment period progressed and three patients out of four with more than 100 days treatment period progressed.

3.4. Safety

No HAP related hematologic toxicity, hepatotoxicity and nephrotoxicity were observed. Non-hematologic HAP related adverse reactions were observed. Transient abdominal discomfort was observed in 2 patients (No.1, No.5) during treatment but symptoms disappeared without any specific treatment. No patient discontinued treatment due to any HAP related adverse events.

3.5. Cases of long survival

Case 1 (No. 2) was a 74-year-old male patient diagnosed with NSCLC on September, 2009. Tumor stage was Ⅳ (T4N3M1a). He received three cycles of chemotherapy (paclitaxel+ cisplatin) from September, 2009 to November, 2009. He failed first-line chemotherapy with significant adverse effects.

Because of his old age and adverse effects, he discontinued conventional therapy and instead received HAP as a Complementary and Alternative Medicine (CAM) from May 7, 2010 to August 26 2010. HAP was administered 6,000 mg daily. His performance status was ECOG 2 at initial administration. Disease was stable on chest CT taken from May 31, 2010 and September 1, 2010. Cancer growth was halted at least 12 weeks (3 months) after the initial administration of HAP. He survived without evidence of progression to date (Oct. 31st 2011).

Case 2 (No.3) was a 74-year-old female patient diagnosed with NSCLC on May, 2010. Tumor stage was Ⅳ (spinal metastasis in T11). She refused conventional therapy and wished to be treated with CAM. She received HAP from June 16, 2010 to August 2, 2011. HAP was received 6,000 mg daily. Her performance status was ECOG 2 at initial administration. Disease was stable on chest CT taken from June 16, 2010 to September 17, 2010. But magnetic resonance imaging (MRI) on September 29, 2010 showed aggravation of spine (T11) metastasis. She received radiation therapy to spine metastasis from

November 16, 2010 and November 22, 2010. She survived without evidence of progression to date (Oct. 31st 2011).

Case 3 (No. 4) was a 47-year-old female patient diagnosed with NSCLC on August 31, 2009. Tumor stage was Ⅳ. She received first-line chemotherapy (gemzar-cisplatin) from September, 2009 to November, 2010. She additionally received second-line chemotherapy (tarceva) from November, 2009 to February, 2010. She received HAP as third-line chemotherapy from April 6, 2010 to December 8 2010. HAP was administered 6,000 mg daily. Her performance status was ECOG 1 at initial administration. Disease was stable on chest CT taken from June 16, 2010 and September 15, 2010. Cancer growth was halted for at least 12 weeks (3 months) after the initial administration of HAP. She survived without evidence of progression to date (Oct. 31st 2011).

Ⅳ. Discussion

This study was designed to investigate the anti tumor effect of HAP in patients with advanced-stage IIIb/Ⅳ NSCLC. Lung cancer is one of the most common malignancy and the leading cause of cancer death worldwide. The prognosis for lung cancer is poor, with a 5-year survival rate of only 15%[27]. Standard treatment for NSCLC, which comprises 80% to 85% of all lung cancer cases, involves surgery, radiation therapy, and chemotherapy[28]. Surgery is the mainstay treatment in patients with localized disease (stage I-II) to accomplish a curative intent.

Chemotherapy is the primary first-line treatment for 70 to 80% of patients who present with locally advanced (stage IIIb) or metastatic (stage IV) disease. In advanced NSCLC, objectives of chemotherapy are prolonged survival, improved quality of life and enhenced symptom control[29]. Standard first-line chemotherapy for patients with good performance status (0/1) is a platinum-based (i.e., cisplatin or carboplatin) doublet regimen incorporating a third-generation cytotoxic agent (e.g., gemcitabine, vinorelbine, paclitaxel, or docetaxel). Carboplatin may be prescribed if the patient is unable or unwilling to receive cisplatin[30].

Although first-line chemotherapy has improved survival of patients with advanced NSCLC, overall and one year survival (8-11 months and 27-47%, respectively) still remain poor[31]. In stage IIIb/IV patients, response to first-line therapy is generally short lived and progression occurs on an average 4-6 months upon discontinuation of the treatment. Patients with stage IIIb/IV NSCLC should receive two to four cycles of chemotherapy and patients with stage IV NSCLC should receive no more than six cycles of chemotherapy[33].

Patients who fail to respond to first-line chemotherapy are recommended second-line chemotherapy. Many of these patients continue to have a good performance status. Recent studies indicate

that 50% of patients receive second-line treatment. Docetaxel or pemetrexed is recommended as second-line therapy for patients with locally advanced or metastatic NSCLC with adequate performance status who have progressed on first-line therapy[34]. In the current review, the objective response rates to chemotherapeutic agents are lower than those in the first-line setting in cases of advanced NSCLC[35].

In recent years, the improved understanding of cancer biology has led to the investigation of several new targeted therapies directed against key biological processes in NSCLC development and progression. These agents, including monoclonal antibodies (bevacizumab) and small-molecule tyrosine kinase inhibitors (erlotinib, gefitinib), have the potential for increased selectivity and thereby reduced toxicity compared with standard chemotherapy[29]. Second-line regimen did not show dramatic breakthroughs from the existing published or ongoing trials. Given the incurable nature of advanced NSCLC, and the modest survival seen in the second-line setting, patient convenience and preference should be considered first when selecting a second-line agent[36].

HAP was developed by East-West Cancer Center (EWCC) in 1996 for anti tumor purpose. HAP is composed of eight products from eight species of Korean medicinal plants and animals (Table I), and has been used in oriental medicine to treat cancer patients with the aim of enhanced immune function and augmentation of vital energy. Reports on Wheel Balance Therapy (WBT), a traditional Korean medical therapy using HAP, had shown positive outcomes in case studies and retrospective studies on lung cancer[19-22, 37-38].

According to prospective study carried out by Jeong et al. in 2010, HAP could prolong the survival rate of inoperable IIIb/Ⅳ NSCLC and be more effective when combined with conventional therapy[22]. Significant prevention of basic fibroblast growth factor (bFGFs)-induced human umbilical vein endothelial (HUVE) cell proliferation, adhesion, migration, and capillary-like tubular network

formation by HAP has been reported[39]. In one study, HAP demonstated significant concentration-dependent inhibition of cell motility and invasiveness of NCI-H460 NSCLC cells. The tight junction (TJ)s and matrix metalloproteinase (MMP)s are critical targets of HAP-induced anti invasive activity[40].

HAP may be a potent chemotherapeutic agent for decreasing the risk of lung cancer development. In advanced cancer clinical trials, the time-honored standard for demonstrating efficacy of new adjuvant therapies is an improvement of OS. It requires phase III trials of large sample size with lengthy follow-ups. Measurement of OS requires extended follow-ups, which may prevent the timely dissemination of results and consequent implementation of effective treatment regimen. The current review provides a perspective on the suitability and validity of PFS as an alternative end point for OS.

PFS is defined as the time from randomization to the first of either recurrence or relapse, second cancer, or death. PFS provides a more biologically relevant measure of a new treatment's impact on the disease process. But PFS does not account for any long-term effects of a treatment such as end-organ toxicities or secondary malignancies that may ultimately adversely impact survival[41]. It is difficult to verify the effects of HAP due to the limitation of short term and fewer subjects study. In this report, we used OS as well as PFS as criteria to evaluate the efficacy of HAP.

Chemotherapy is classified into first line and over second line. Although first-line chemotherapy for patients with advanced NSCLC has improved survival, overall and one year survival (8-11 months and 27-47%, respectively) remain poor[31-32]. In cases of over second line chemotherapy, chemoagents are docetaxel, erlotinib, gefitinib, pemetrexed, etc. The impact of second-line chemotherapy has been studied in a large cohort of 4,318 patients in 19 phase III trials. The median survival time was 6.6 months[35]. The vast majority of chemotherapy guidelines recommend docetaxel or pemetrexed for stage IIIb/IV NSCLC patients who fail first-line chemotherapy[33-34].

Docetaxel (75 mg/m^2 every 3 weeks) significantly prolonged median survival, one year survival and median PFS duration in comparison with best supportive care (median survival 7.5 versus 4.6 months; median PFS 2.1 versus 1.6 months; one year survival 37 versus 12%)[41]. In this study, six patients participated and resulted in median survival of 13.2 months (397 days), median PFS 3.2 months (96 days) and one year survival rate was 66.7%. HAP-treated patients showed significantly better median OS, median PFS, one year survival rate than best supportive care group as well as docetaxel-treated patients. However the results of this study could not be directly compared with results of other studies due to several limitations. The results suggest the potential of HAP as a second-line or over regimens for stage IIIb/IV NSCLC patients who fail chemotherapy.

In the safety aspect, chemotherapy cause hematological toxicity such as febrile neutropenia and thrombocytopenia whereas nonhematological toxicity includes diarrhea, asthenia and nausea. In this study, no HAP related hematologic toxicity, hepatotoxicity and nephrotoxicity were observed. Non-hematologic HAP related adverse reactions were not observed. Transient abdominal discomfort was observed in 2 patients (N0.1, N0.5) during the treatment but symptoms disappeared without any specific treatment. No patient has discontinued HAP therapy due to adverse effect in this study.

HAP treatment showed longer OS and PFS than previous clinical studies with no significant adverse events. But this study may have several limitations to prove the efficacy of HAP: (1) small numbers of patients, (2) short and variable HAP treatment period, (3) different treatment history of individual patients and (4) limitation of regular and continuous follow-ups.

In conclusion, HAP is worth investigating as a second-line or over regimens for stage IIIb/IV NSCLC patients who fail chemotherapy. But its effect has not yet been confirmed. In the future, additional controlled clinical trials with larger samples from multi-centers are warranted to further evaluate the efficacy and safety of HAP.

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Survival Outcomes in Patients with Advanced-Stage IIIb/Ⅳ Non-small Cell Lung Cancer Treated with *HangAm-Plus*

Abstract

Background and Objective Non-small cell lung cancer (NSCLC) represents approximately 80% of lung cancers. Unfortunately, at the time of diagnosis, most patients have advanced, surgically unresectable disease with a very poor prognosis. Oriental herbal medicine, HangAm-Plus (HAP), has been developed for anti tumor purpose and several previous studies have already reported its therapeutic effects. The goal of this study is to evaluate the efficacy of HAP as a second-line over treatment of advanced-stage IIIb/Ⅳ NSCLC.

Methods The study involved six patients treated in East-West Cancer Center (EWCC) from April 2010 to October 2011. Inoperable advanced-stage IIIb/Ⅳ NSCLC patients received 3,000 or 6,000 mg of HAP on daily basis over a 12-week period. Computed tomography (CT) scan was obtained from patients at both initial administration of HAP and after 12 weeks of treatment. We have observed and analyzed their overall survival (OS) and progression-free survival (PFS).

Results Of the six participating patients, three expired during the study period. OS ranged from 234 to 512 days with median survival of 397 days and one year survival rate of 66.7%. Three remaining patients survived as of October 31, 2011. In the 12-weeks-interval chest CT assessment, three patients had stable disease (SD) and other three patients had progressive disease (PD). Patients with SD had longer

overall survival than patients with PD. No significant OS variation correlated with administration period. PFS of patients ranged from 88 to 512 days and median PFS is 96 days. Patients with SD show longer PFS period than patients with PD. There is no significant PFS variation according to administration period. Although results of this study cannot be directly compared with results of other studies, OS and PFS were greater than those of the docetaxel or best supportive care group.

Conclusion HAP may prolong the OS and PFS of inoperable stage IIIb/Ⅳ NSCLC patients without significant adverse effects. In the future, more controlled clinical trials with larger samples from multi-centers are warranted to evaluate the efficacy and safety of HAP.

KEY WORDS:
Non-small cell lung cancer; HangAm-Plus(HAP) ; Overall survival; Progression-free survival.

항암플러스로 치료받은 IIIb/Ⅳ기 진행성 비소세포성폐암 환자의 생존율에 대한 분석

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초 록

비소세포성 폐암은 전체 폐암의 80%를 차지하고, 대부분의 환자들은 수술이 불가능한 진행된 병기로 진단되며, 매우 불량한 예후를 나타내는 특징이 있다. 항암플러스는 항종양을 목적으로 개발된 한약 제제로, 기존의 여러 연구에서 이미 그 효과가 밝혀졌다. 본 연구의 목적은 IIIb/Ⅳ기의 진행성 비소세포성 폐암에 대한 2차 이상의 치료제로써의 항암플러스(HangAm-Plus : HAP)의 효능을 관찰하는 것이다.

2010년 4월부터 2011년 10월까지 동서암센터에서 HAP로 치료받은 수술이 불가능한 IIIb/Ⅳ기의 비소세포성폐암 환자 6명이 본 연구에서 관찰되었다. 환자들은 매일 3회에 걸쳐 총 3,000 혹은 6,000 mg의 HAP를 복용하였다. HAP를 최초 복용하는 시점과 투약 12주 경과 시점에 종양 반응평가를 위해 흉부 컴퓨터 단층촬영(computed tomography, CT)을 실시하였다. 또 2011년 10월까지의 환자들의 전체 생존 기간(overall survival, OS), 무진행 생존기간(progression-free survival, PFS) 및 1년 생존률을 분석하였다.

마지막 추적일은 2011년 10월 31일이었다. 관찰 기간 중 6명의 환자 중 3명의 환자가 사망하였고, 생존 기간은 234일에서 512일에 분포하였다. 그리고 전체 생존 중앙값은 13.2주(397일)였으며 1년 생존율은

66.7%였다. 투약 후 12주 시점에서 시행된 흉부 CT에서 3명의 환자가 안정병변(stable disease : SD)을 보였고, 3명의 환자는 진행병변(progressive disease : PD)을 보였다. SD를 보인 환자들은 PD를 보인 환자들보다 생존기간이 길게 나타났고. HAP의 투약기간에 따른 생존기간의 명확한 차이는 없었다. 환자들의 무진행 생존 중앙값은 88일에서 512일로 분포했으며, 평균 무진행 생존기간은 3.2주(96일)였다. SD를 보인 환자들이 PD를 보인 환자들에 비해서 무진행 생존기간이 길게 나타났다. HAP 복용기간에 따른 무진행 생존기간의 차이는 관찰되지 않았다. 본 연구의 결과가 기존의 연구에 직접 비교하기는 어렵지만, 최선의 보존적 치료는 물론이고 우선적인 2차 선택약인 도세탁셀의 생존 기간(7.5주)과 무진행 생존기간(2.1주)보다 우수함을 보였다. HAP와 관련된 혈액학적 및 비혈액학적 부작용은 관찰되지 않았다.

본 연구에서는 HAP는 수술이 불가능한 IIIb/Ⅳ기의 비소세포성폐암 환자에의 생존 기간, 무진행 생존기간을 연장할 수 있는 가능성을 보였다. HAP의 효과 및 안전성을 재평가하기 위해, 향후 다기관의 큰 모집단을 대상으로 한 보다 엄격히 설계된 연구가 요망된다.

핵심어
비소세포성 폐암; 항암플러스; 생존기간; 무진행 생존기간.