

RESEARCH COMMUNICATION

Cisplatin-Based Therapy for the Treatment of Elderly Patients with Non-Small-Cell Lung Cancer: a Retrospective Analysis of a Single Institution

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Abstract

Background: In spite of the fact that platinum-based doublets are considered the standard therapy for patients with advanced non-small-cell lung cancer (NSCLC), no elderly-specific platinum based prospective phase III regimen has been explored. The aim of this retrospective singlecenter study was to evaluate the efficacy and side effects of cisplatin-based therapy specifically for the elderly. **Methods:** Patients receiving platinum-based treatment were divided into three groups. In the first group (GC), Gemcitabine was administrated at 1000 mg/m² on days 1, 8 and cisplatin was added at 75 mg/m² on day 1. In the second group (DC), 75 mg/m² docetaxel and cisplatin were administered on day 1. The third group (PC) received 175 mg of paclitaxel and 75 mg of cisplatin on day 1. These treatments were repeated every three weeks. **Result:** GC arm had 36, the DC arm 42 and the PC arm 29 patients. Grade III-IV thrombocytopenia was higher in the GC arm (21.2% received GC, 2.8% received DC, and 3.8% received PC), while sensory neuropathy was lower in patients with GC arm (3.0%, 22.2%, and 23.1% received GC, DC and PC, respectively). There were no statistically significant difference in the response rates among the three groups (p>0.05). The median Progression-free survival (PFS) was 5.0 months and the median Overall survival (OS) in each group was 7.1, 7.4 and 7.1 months, respectively (p>0.05). **Conclusion:** The response rate, median PFS and OS were similar among the three treatment arms. Grade III-IV thrombocytopenia was higher in the GC arm, while the GC regimen was more favorable than the other cisplatin-based treatments with regard to sensory neuropathy.

Keywords: Advanced lung cancer - elderly patients - first line chemotherapy - cisplatin based therapy

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Introduction

Lung cancer is the most common among cancer-related deaths in Western countries (Parkin, 2001). Non-small cell lung cancer (NSCLC) represents between 80% to 85% of all lung cancers cases.

At the time of diagnosis, In two-third of patients with lung cancer have locally advanced or metastatic diseases. The overall 5-year survival rate among these patients population are under 10% (Shepherd, 1993; Walling, 1994). Data from the Surveillance, Epidemiology, and End Results (SEER) Program data in the United States show that the median age at diagnosis in NSCLC patients is 69 years (Havlik et al., 1994).

Elderly cancer patients present with physiological changes in organ functions, and drug pharmacokinetics. Thus, lung cancer in the older individual is frequently undertreated. For this reason, lung cancer in the elderly patients is a progressively widespread problem faced by the oncologist (Repetto et al., 2003; Maione et al., 2010). The Elderly Lung Cancer Vinorelbine Italian Study Group (ELVIS) showed that single-agent vinorelbine

improved survival and quality of life (QOL) compared with supportive care alone (median survival time, 6.4 months and 4.8 months, p=0.04) (The Elderly Lung Cancer Vinorelbine Italian Study Group, 1999).

In spite of the fact that platinum-based doublets are considered the standard therapy for patients with advanced NSCLC, no elderly-specific platinum based prospective phase III study has been explored. Nonetheless, retrospective subgroup analyses of several phase III trials for elderly patients have been done (Kelly K et al., 2001; Langer et al., 2002; Hensing et al., 2003; Belani et al., 2005; Sederholm et al., 2005; Ansari et al., 2007). In these studies it was indicated that PFS, OS and response rate were not significantly superior between age groups. Grade 3-4 toxicities for elderly patients, some studies were higher (Langer et al., 2002; Belani et al., 2005; Sederholm et al., 2005; Ansari et al., 2007), whereas others were not observed (Kelly et al., 2001; Hensing et al., 2003).

In the present study we performed a retrospective analysis of the efficacy and side effects of cisplatin-based therapy for the treatment of Turkish elderly patients with NSCLC.

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Materials and Methods

Patient Population

We retrospectively reviewed 107 locally advanced or metastatic lung cancer patients who were treated cisplatin-based therapy as first-line treatment from January 2005 to October 2011 in Dicle University School of Medicine, Division of Medical Oncology.

They met the following inclusion criteria; 1) they were 65 years or older in age; 2) they had histologic or cytologic diagnosis of locally advanced and/or metastatic NSCLC; 3) no previous chemotherapy or radiotherapy; 4) they had to have measurable disease, as defined by Response Evaluation Criteria in Solid Tumors (RECIST).

Treatment and Assessment

Patients receiving platinum-based treatment were divided into three groups. The first group (GC); Gemcitabine was administered at 1000 mg/m² on days 1, 8 and cisplatin was added at 75 mg/m² on day 1 every 21-day cycle. In the second group (DC), 75 mg/m² docetaxel and cisplatin were administered on day 1. The third group (PC) received 175 mg of paclitaxel and 75 mg of cisplatin on day 1. These treatments were repeated every three weeks.

This study was used WHO toxicity criteria and we recorded grade III-IV toxicity. Imaging studies were documented by computed tomography at baseline and every three cycles for patients.

The responses to chemotherapy were measured according to Response Evaluation Criteria in Solid Tumors (RECIST). A complete response (CR) was defined as disappearance of all target lesions, no new lesions. A partial response (PR) was defined as at least a 30% decrease in the sum of the longest diameter of the measurable lesions. Progression was defined as at least a 20% increase in the sum of longest diameter of the measurable lesions. Stable disease (SD) was defined as small changes.

Statistical Analysis

All of the analyses were performed using the SPSS statistical software program package (SPSS version 11.0 for windows). The differences of the clinical characteristics among three treatment arms were analyzed by a Fisher's exact test. OS and PFS were calculated with the log-rank test. The Kaplan–Meier method was used to draw survival curves. Differences were assumed to be significant when P value of less than 0.05.

Results

Patient Characteristics

Between January 2005 to October 2011, 107 locally advanced or metastatic lung cancer patients who were administered cisplatin-based therapy as first-line treatment were enrolled in this study

The patients' baseline characteristics are listed in Table 1. GC arm 36 (M: 33, F: 3), DC arm 42 (M: 38, F: 4) and PC arm 29 (M: 23, F: 6), were patients. Performance status in a PC arm was better than the other groups. Rate

Table 1. The General Characteristics of the Patients

Characteristic	GC	DC	PC	p
Enrolled patients	36	42	29	
Sex				
Male	33	38	23	
Female	3	4	6	
Median age, years	69.4	70.0	70.0	P>0.05
Performance status (%)				
0-1	57.1	56.0	68.0	
2-3	42.9	44.0	32.0	P>0.05
The number of cycles (median)	3.5	5.0	4.0	P>0.05
Stage (%)				
III	41.7	26.2	20.7	P=0.001
IV	58.3	73.8	79.3	
Histology (%)				P>0.05
Squamous	62.5	79.2	50.0	
Adenocarcinoma	33.3	20.8	43.8	
Other	4.2	0	6.2	
PFS (median, month)	5.0 (1-15)	5.0 (1-23)	5.0 (1-27)	P>0.05
OS (median, month)	7.1 (1-29)	7.4 (1-58)	7.1 (2-32)	P>0.05

Table 2. The Characteristics

Characteristic	GC (%)	DC (%)	PC (%)	p
Toxicity profile of grade 3 to 4;				
Hematologic toxicity :				
Neutropenia	39.4	33.3	30.8	P>0.05
Febrile neutropenia	9.7	2.5	8.7	P>0.05
Thrombocytopenia	21.2	2.8	3.8	P=0.02
Anemia	12.1	19.4	15.4	P>0.05
Nonhematologic toxicity :				
Nausea /Vomiting	21.2	30.6	29.2	P>0.05
Diarrhea	3.0	0	7.7	P>0.05
Sensory neuropathy	3.0	22.2	23.1	P=0.02
Treatment efficacy of the patients;				
Response				
Complete response	0	2.8	0	P>0.05
Partial response	36.7	38.9	33.3	P>0.05
Stable disease	40.0	41.7	40.8	P>0.05
Progressive disease	23.3	16.6	25.9	P>0.05
Response rate (CR + PR)	36.7	41.7	33.3	P>0.05

of patients with stage III was higher in the GC arm (41.7%, 26.2%, and 20.7% received GC, DC and PC, respectively). Among patients with the three groups, gender, age, the number of cycles and histology did not have a statistically difference (p>0.05).

Safety Results

The toxicities of grade 3 to 4 was seen during treatment are shown in Table 2. Neutropenia was the most common significant hematologic toxicity and nausea- vomiting was the most common nonhematologic toxicity in among treatment arms. Grade III-IV thrombocytopenia was higher in the GC arm (21.2% received GC, 2.8% received DC, and 3.8% received PC), while sensory neuropathy was lower in patients with a GC arm (3.0%, 22.2%, and 23.1% received GC, DC and PC, respectively).

Efficacy

Treatment efficacy was shown in Tables 2. There were no statistically significant difference in the response rate among the three groups (p>0.05).

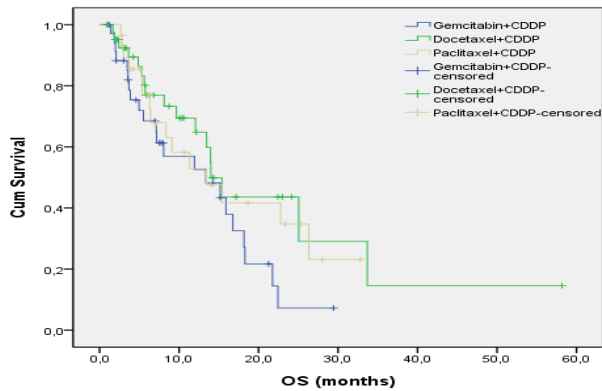


Figure 1. Kaplan-Meier Estimates of OS Curve ($p>0.05$)

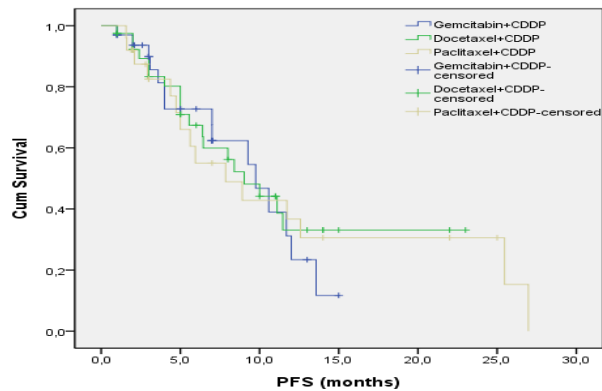


Figure 2. Kaplan-Meier Estimates of PFS Curve ($p>0.05$)

The median PFS was 5.0 months in the three groups (Figure 1). The median OS in each group was 7.1, 7.4 and 7.1 months, respectively ($p>0.05$) (Figure 2).

Discussion

In spite of the fact that platinum-based doublets are considered the standard therapy for patients with advanced NSCLC, no elderly-specific platinum based prospective phase III study has been explored. To improve therapeutic efficacy, retrospective subgroup analyses of several phase III trials have investigated platinum-based treatment for elderly patients with advanced NSCLC (Kelly et al., 2001; Langer et al., 2002; Hensing et al., 2003; Belani et al., 2005; Sederholm et al., 2005; Ansari et al., 2007). In these studies were indicated that PFS OS, and response rate were not significantly superior between age groups. Grade 3-4 toxicities for elderly patients, some studies were higher (Langer et al., 2002; Belani et al., 2005; Sederholm et al., 2005; Ansari et al., 2007), whereas others were not observed (Kelly K et al., 2001; Hensing et al., 2003). We performed a retrospective analysis of the efficacy and side effects of cisplatin-based therapy for the treatment of elderly patients with NSCLC.

Previous studies had showed that platinum-based treatment induced a objective response of 22% to 50% and median OS were 5.8 to 12.6 months (Pallis et al., 2010). In our study, the rate of objective response showed that platinum-based treatment induced an objective response of 33.7% to 41.7% (36.7% received GC, 41.7% received DC, and 33.3% received PC) and median OS were 7.1 to

7.4 months (7.1, 7.4, and 7.1 received GC, DC and PC, respectively). The median PFS was 5.0 months in the three groups.

The side effects of cisplatin-based therapy for the treatment of elderly patients are especially special concern. Nevertheless, toxicity profile opposite age groups was usually consistent in the literature. Some clinical trials indicated that hematologic toxicity of grade 3 to 4 was higher in elderly patients (Rocha et al., 2002; Schild et al., 2003; Sequist et al., 2003; Jatoi et al., 2005), while the other trials were not (Hensing et al., 2003; Langer et al., 2003; Ansari et al., 2011). Ageing is associated with decreasing in bone marrow reserve and myelotoxicity may be fairly increased (Deppermann et al., 2001). On the other hand, compared with younger patients who receive taxane-based therapy have great risk for developing peripheral neuropathy in older patients (Hensing et al., 2003; Nurgalieva et al., 2010). In our retrospective study, Grade III-IV thrombocytopenia was higher in the GC arm (21.2% received GC, 2.8% received DC, and 3.8% received PC, respectively, $p=0.02$), while sensory neuropathy was lower in patients with a GC arm (3.0%, 22.2%, and 23.1% received GC, DC and PC, respectively, $p=0.02$).

The present study has got some limitations. The one of the limitations is retrospective nature, the other is small sample.

In conclusion, the response rate, median PFS and OS are similar in among three treatment arms. Grade III-IV thrombocytopenia was higher in the GC arm, while the GC regimen was more favorable than the the other cisplatin-based therapy for sensory neuropathy. For this reason, prospective and larger clinical trials are needed to define the efficacy and side effects of cisplatin-based therapy for the treatment of elderly patients with NSCLC.

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