Tanaffos (2011) 10(3), 20-23

Consolidation Chemotherapy with Docetaxel after Platinum-Based Chemotherapy in Patients with Non-Small Cell Lung Cancer: A Preliminary Report

Hamid Attarian, Hamid Rezvani, Mojtaba Ghadyani, Faezeh Eshaghi

Department of Hematology and Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

ABSTRACT

Background: *The efficacy of second line chemotherapy for relapsed non small cell lung cancer has been established. In this study, we evaluated the efficacy and toxicity of maintenance therapy with docetaxel in patients with non-small cell lung cancer who were stabilized with first line chemotherapy and had good performance status before relapse. The primary objective was to determine one-year survival and the other objectives were evaluation of adverse effects and time to progression.*

Materials and Methods: *Eighteen patients with lung cancer were included in this study. All patients were at stage III and IV, without distant metastasis or neuropathy. All patients had been treated with platinum based regimen initially and were responsive or stable with no progression. The patients were treated with docetaxel 75 mg/m^2 for a total of 4 cycles repeated every 3 weeks.*

Results: *All patients accomplished 4 chemotherapy cycles and a total of 72 cycles were administered. The mean time of progression free survival (PFS) was 9-10 months and one- year survival (OS) was 94.4% without any significant adverse effect necessitating medical intervention. The mean survival time of patients was 18 (12-20) months.*

Conclusion: *Using docetaxel as consolidation chemotherapy in patients with non small cell lung cancer can prolong time to progression of disease and probably patients' survival without significant adverse effects or negative impact on the quality of life.* ***(Tanaffos2011; 10(3): 20-23)***

Key words: *Non small cell lung cancer, Consolidation chemotherapy, Docetaxel*

INTRODUCTION

The efficacy of chemotherapy in improving survival of patients with non-small cell lung cancer at all stages has been reported in several studies, including a meta-analysis on 52 randomized clinical trials (1). These results are especially noticeable in more advanced stages of lung cancer. Since the new drugs and more active components have not been used in clinical trials yet, it is possible to find more satisfying results in future studies. Recently, published randomized trials have shown that using regimens with newer generations of drugs was

Correspondence to: Rezvani H

Address: Department of Hematology and Oncology, Taleghani General Hospital, Chamran Highway, Tehran, Iran

Email address: hampegrad@yahool.com

Received: 17 February 2011

Accepted: 14 June 2011

associated with 40% response rate and one year survival of 35-40% (2). Several studies indicate that the maximum benefit of chemotherapy in non-small cell lung cancer patients will be achieved after 3-4 cycles (3), and it seems that there is no further benefit for long term chemotherapy with platinum-based regimens (4).

In fact, if disease progression occurs after completion of first line chemotherapy, administration of another drug which has not been used in first line chemotherapy is recommended. The recommended drugs for second line regimen are erlotinib, docetaxel and pemetrexed all of which have been approved by FDA to be used in second line chemotherapy (5).

There are many studies in the literature on the efficacy of second line regimen including consecutive or maintenance therapy; however, the proper time of initiation and duration of this type of treatment is not clear (6).

In this study, we evaluated the efficacy and safety of therapy with docetaxel after completion of platinum-based regimen for non small cell lung cancer.

MATERIALS AND METHODS

In this case series study, we recruited 18 patients with non small cell lung cancer. All patients were at stage III and IV, without distant metastasis or neuropathy. All patients had been treated with 6 cycles of platinum-based regimen before entering the study. Patients who were partially or fully responsive to first line treatment or had stable disease were eligible to enter the study. Patients with performance status > 2 were excluded from the study. Patients were selected with simple random selection method. The response to therapy was defined based on "Response Evaluation Criteria in Solid Tumors" (RECIST) criteria: complete response is defined as complete remission of lesions; response is defined as at least 30% reduction in lesion size; stable disease is defined as no change in lesion size and advanced disease is defined as at least 20% increase in lesion size or emergence of new lesions.

Patients were treated with docetaxel 75 mg/m^2 for a total of 4 cycles repeated every 3 weeks. Physical examination, chest x-ray, CBC and blood biochemistry analysis including renal and liver function tests were performed for all patients every 3 weeks. Computed tomography scan was performed at the end of 6^{th} and 12^{th} weeks. All patients were followed for 20 months after the end of treatment.

Data analysis

Data were analyzed using SPSS software version13. The response to therapy was defined based on RECIST criteria. One year survival was determined by Kaplan–Meier method. The comparison between stratified variables was performed using Pearson X^2 test. The correlation between continuous variables was determined by independent sample t-test for variables with normal distribution and with Mann-Whitney test for variables without normal distribution.

RESULTS

A total number of 18 patients with stage III and IV lung cancer were evaluated. The mean age of patients was 60.6 ± 7.6 (range: 42-71) years. There were 12 male (66.7%) and 6 female (33.3%) patients. The rate of complete response was 77%; 12 patients (66.7%) had partial response, 2 patients (11.1%) had complete response and 4 patients (22.2%) had stable disease (Table 1).

Table 1. Frequency of response to therapy

Treatment response	Frequency	Percentage
Partial response	12	66.7
Complete response	2	11.1
Stable disease	4	22.2
Total	18	100.0

The rate of partial response in males and females was 58.3% and 83.3% respectively; although there was no significant difference between males and females regarding response to therapy (P=0.314). The time to progression ranged from 3 to 14 months (mean 9.4 ± 2.2). Median time to progression (TTP) in males was 9.25 months (range 3-11) and in females was 10.5 (range 7-14) months (Table 2). Median time to progression in patients with partial response, complete response and stable disease was 10 (range 3-14), 8.5 (range 7-10), and 9 (range 8.5-10) months, respectively. One year survival in patients who received docetaxel was 94.4% and mean survival rate ranged from 12 to 22 months (mean 18.4±2)(Figure 1)

Table 2. Time to progression of non small cell lung cancer based on sex.

Gender	N	Mean	SD	Median	Minimum	Maximum
Female	6	10.3333	2.33809	10.5000	7.00	14.00
Male	12	8.9583	2.06109	9.2500	3.00	11.00
Total	18	9.4167	2.19123	9.7500	3.00	14.00

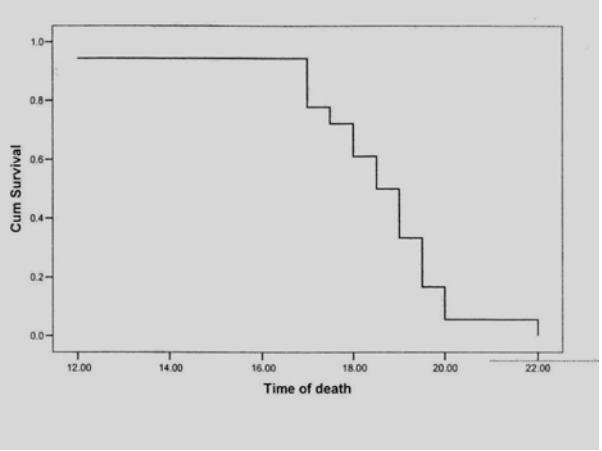

Figure 1. Survival of patients with non small cell lung cancer who underwent chemotherapy regimen with docetaxel

The average number of 4 cycles of docetaxel was administered. Generally, no dose modification due to adverse effects was performed for patients. The most common hematologic adverse effect was anemia (14 patients). Also, grade I or II neuropathy occurred in 8 patients and thrombocytopenia in 2 patients. Fever and neutropenia did not occur in any patient.

DISCUSSION

This study showed that adding docetaxel as consolidation therapy in patients with non-small cell lung cancer prolongs time to progression to 3 -14 months (mean 9.4±2). Initial studies did not demonstrate that consecutive or maintenance chemotherapy after first line treatment can increase overall survival (7, 8). Buccheri et al. could not show any improvement in the overall survival rate of patients with stable disease whose treatment was continued by administering adriamycin, cyclophosphamide and lomustine (9). Also, the adverse effect of therapy increased and the quality of life decreased in this group of patients.

In another study, Westeel et al. used vinorelbine as a conservative therapy and compared it with supportive therapy after first line treatment and found no significant difference between OS and PFS of patients (10). Moreover, Brodowicz et al. showed that continuing therapy with gemcitabine after first line treatment with cisplatin and gemcitabine regimen will increase the time before progression (11).

In the TAX 320 non-small cell lung cancer study, patients who had received agents such as paclitaxel also benefited from maintenance docetaxel. The highest survival was observed in docetaxel group and 30% of patients were alive for one year, comparing to 21% in vinorelbine and 19% in ifosfamide groups (12). In Fidias et al. study, a noticeable improvement of PFS (for 3 months) was noted in patients who received docetaxel and even, the OS increased for 2.6 months; although it was not statistically significant (13).

In our study, the PFS was 9-10 months which is in average range. This finding is very noticeable when compared with historical control groups and may be caused by using different drugs in first line treatment. The increase in one year survival that was noted in 94% of our patients may be caused by smaller number of patients that we recruited.

But the most important feature of our study was that no significant side effect necessitating hospitalization occurred and all patients could complete the treatment period. It emphasizes that if the physicians start treatment as soon as possible, the patients will better tolerate it.

However, considering the results of our study and other similar studies, we can conclude that if patients with non-small cell lung cancer respond to treatment initially and become stable; continuing the treatment with a medication other than the first line drugs may increase the PFS minimally. Higher number of patients and newer drugs such as pemetrexed have to be evaluated in future studies; hopefully, this way the OS may increase.

REFERENCES

1. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomised clinical trials. Non-small Cell Lung Cancer Collaborative Group. ***BMJ*** 1995; 311 (7010): 899- 909.
2. Shepherd FA. Chemotherapy for non-small cell lung cancer: have we reached a new plateau? ***Semin Oncol*** 1999; 26 (1 Suppl 4): 3- 11.
3. Lustberg MB, Edelman MJ. Optimal duration of chemotherapy in advanced non-small cell lung cancer. Curr ***Treat Options Oncol*** 2007; 8 (1): 38- 46.
4. Socinski MA, Stinchcombe TE. Duration of first-line chemotherapy in advanced non small-cell lung cancer: less is more in the era of effective subsequent therapies. ***J Clin Oncol*** 2007; 25 (33): 5155- 7.
5. Shepherd FA, Dancey J, Ramlau R, Mattson K, Gralla R, O'Rourke M, et al. Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy. ***J Clin Oncol*** 2000; 18 (10): 2095- 103.
6. Grossi F, Aita M, Follador A, Defferrari C, Brianti A, Sinaccio G, et al. Sequential, alternating, and maintenance/consolidation chemotherapy in advanced non-small cell lung cancer: a review of the literature. ***Oncologist*** 2007; 12 (4): 451- 64.
7. Smith IE, O'Brien ME, Talbot DC, Nicolson MC, Mansi JL, Hickish TF, et al. Duration of chemotherapy in advanced non-small-cell lung cancer: a randomized trial of three versus six courses of mitomycin, vinblastine, and cisplatin. ***J Clin Oncol*** 2001; 19 (5): 1336- 43.
8. Sculier JP, Lafitte JJ, Lecomte J, Alexopoulos CG, Van Cutsem O, Giner V, et al. A phase III randomised trial comparing sequential chemotherapy using cisplatin-based regimen and paclitaxel to cisplatin-based chemotherapy alone in advanced non-small-cell lung cancer. ***Ann Oncol*** 2007; 18 (6): 1037- 42.
9. Buccheri GF, Ferrigno D, Curcio A, Vola F, Rosso A. Continuation of chemotherapy versus supportive care alone in patients with inoperable non-small cell lung cancer and stable disease after two or three cycles of MACC. Results of a randomized prospective study. ***Cancer*** 1989; 63 (3): 428- 32.
10. Westeel V, Quoix E, Moro-Sibilot D, Mercier M, Breton JL, Debieuvre D, et al. Randomized study of maintenance vinorelbine in responders with advanced non-small-cell lung cancer. ***J Natl Cancer Inst*** 2005; 97 (7): 499- 506.
11. Brodowicz T, Krzakowski M, Zwitter M, Tzekova V, Ramlau R, Ghilezan N, et al. Cisplatin and gemcitabine first-line chemotherapy followed by maintenance gemcitabine or best supportive care in advanced non-small cell lung cancer: a phase III trial. ***Lung Cancer*** 2006; 52 (2): 155- 63.
12. Fossella FV, DeVore R, Kerr RN, Crawford J, Natale RR, Dunphy F, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small-cell lung cancer previously treated with platinum-containing chemotherapy regimens. The TAX 320 Non-Small Cell Lung Cancer Study Group. ***J Clin Oncol*** 2000; 18 (12): 2354- 62.
13. Fidias PM, Dakhil SR, Lyss AP, Loesch DM, Waterhouse DM, Bromund JL, et al. Phase III study of immediate compared with delayed docetaxel after front-line therapy with gemcitabine plus carboplatin in advanced non-small-cell lung cancer. ***J Clin Oncol*** 2009; 27 (4): 591- 8.