



## Research Article

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# What was the Effect of Taxol in Non-Metastatic Non-Small Cell Lung Cancer Patients in Mansoura University Hospital?



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## Abstract

**Introduction:** Lung cancer has been turned from a rare disease to a worldwide problem. Non-small cell lung cancer (NSCLC) is the most commonly diagnosed type of lung cancer forming about 85% of all cases. Measures for treatment in NSCLC include: surgical resection, radiotherapy, chemotherapy and targeted therapy. They can be used as solo modality or in combination. Taxanes as paclitaxel and docetaxel are important classes of chemotherapeutic agents.

**Aim of the work:** The aim of our retrospective study is to evaluate the role of taxol based chemotherapy in treatment of non-metastatic NSCLC.

**Patient & methods:** Between January 2008 and December 2013, thirty five patients with newly diagnosed, non- metastatic NSCLC were included for this analysis. Between January 2008 and December 2013, thirty five patients with newly diagnosed, non- metastatic NSCLC were included for this analysis. The patients received paclitaxel containing regimens. All were combined either with carboplatin (33 patients) or with cisplatin (2 patients).

**Results:** As regard response rate only one patient achieved complete response, partial response was detected in 18 patients, stationary disease was demonstrated in 12 patients and 4 patients had progressive disease. The most common toxicity was the hematological toxicity. The median PFS was 8 months (95% Confidence Interval, 6.774 -9.226 months). The median OS was 13 months (95% Confidence Interval, 10.533 -15.467 months).

**Conclusion:** Taxol is active class of chemotherapeutic agents in NSCLC and well tolerated.

**Keywords:** Lung cancer; Taxanes; NSCLC; Chemo-radiotherapy; Taxol

**Abbreviations:** NSCLC: Non-Small Cell Lung Cancer; ECOG: Eastern Cooperative Oncology Group; NCI-CTCAE: Common Terminology Criteria for Adverse Events; SPSS: Statistical Package for Social Sciences; PFS: Progression Free Survival; OS: Overall Survival; RR: Response Rate; CR: Complete Response; PR: Partial response; SD: Stationary Disease

## Introduction

Lung cancer has been turned from a rare disease to a worldwide problem. The deaths in USA were 160,340 in 2012 due to lung cancer. In USA, it was responsible for 28% of all cancer mortality. Changing the location does not affect markedly the global lung cancer mortality, with 43% of deaths occurring in more developed countries and 57% occurring in the developing regions Ridge et al. [1]. Non-small cell lung cancer (NSCLC) is the most commonly diagnosed type of lung cancer forming about

85% of all cases. It grows up and spreads much slowly than small cell lung cancer Barzi & Pennell [2]. At diagnosis, more than 80% have locally advanced stage III or stage IV tumor and are not candidate for curative surgery. Five year survival is less than 10% in this patient population Treat et al. [3]. The one year survival rate for lung cancer increased from 35% in between 1975 and 1979 to 42% in 1988 up to 2008. Five year survival rate for lung cancer is poor. The overall 5-year survival rate

for lung cancer of all stages was 16.8% in 2004 and increased slightly over time, in comparison with a 13.3% 5-year survival rate in 1982 Ridge et al. [1].

Measures for treatment in NSCLC include: surgical resection, radiotherapy, chemotherapy and targeted therapy. They can be used as solo modality or in combination depending on the disease status Ravenel [4]. Treatment options for resectable locally advanced NSCLC include radical chemo-radiotherapy and induction neo-adjuvant therapy followed by surgery Thomas et al. [5]. Combination chemotherapy is the standard of care for patients with locally advanced non-resectable NSCLC and a performance status score of 0 or 1 Ramalingam & Belani [6]. Taxanes as paclitaxel and docetaxel are important classes of chemotherapeutic agents McGrogan et al. [7]. The aim of our retrospective study is to evaluate the role of taxol based chemotherapy in treatment of non-metastatic NSCLC in the term of response rate (RR) and toxic profile then to assess progression free survival (PFS) and overall survival (OS).

### Patients and Methods

#### Patient Inclusion Criteria

- Patients were aged 18 to 70 years.
- Performance status  $\leq 2$ .
- Pathologically proven non-small cell lung cancer.
- Non metastatic disease.
- Adequate bone marrow, liver, and kidney functions (haemoglobin  $\geq 9$ g/dl, platelet  $\geq 100,000$ /l, WBCs  $\geq 3000$ /l provided that absolute neutrophil count (ANC)  $\geq 1500$ /l and serum creatinine  $\leq 1.5$  upper limit of normal).
- No prior treatment with chemotherapy.

This study was approved by the Ethical Committee of Faculty of Medicine, Mansoura University. The collected data from patient's sheets included the history from all patients as age, sex and smoking habit. General examination was done including weight, height and surface area. Performance status was assessed according to Eastern Cooperative Oncology Group (ECOG). Tumor staging for all patients were documented according to TNM staging system. Investigations included pathological, radiological and laboratory investigations.

#### Treatment Regimens

Thirty five patients were included in this study. The patients received paclitaxel containing regimens. All were combined either with carboplatin (33 patients) or with cisplatin (2 patients). In most of patients the schedule of paclitaxel used was ranged from 175 -200 mg/m<sup>2</sup> IV infusion over 3 h every 3 weeks, only 4 patients received paclitaxel 75 mg/m<sup>2</sup> IV infusion weekly. The number of cycles ranged from 4 to 8 and the median number was 6. All patients were received pre-medications as

recommended. Symptoms and signs of toxicities were assessed either hematological toxicities or non-hematological toxicities. Toxicities were reported according to the Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.0. The primary end point in our research was to assess the RR and the toxic profile and the secondary end points were to assess PFS and OS.

### Statistical Analysis

The data was collected, coded, processed and analyzed using SPSS (statistical package for social sciences) version 16. Qualitative data were described using number and percent. Associations between categorical variables were tested using Chi-square test ( $\chi^2$ ). Monte Carlo test was used whenever there was one or more cell counted 5 or less. Continuous variables were presented as mean  $\pm$  SD (standard deviation) and Median (min - max). The two groups were compared with Student t test (parametric data) P-value considered significant if  $\leq 0.05$ . The survival functions were tested using Kaplan-Meier.

### Results

Table 1: Patients and tumors characteristics.

Parameter	No. (%) total=35
<b>Age in years</b>	
Median (min - max)	55 (29 - 70)
Age < 60 y	23 (65%)
$\geq 60$ y	12 (35 %)
<b>Sex</b>	
Male	20 (57%)
Female	15 (43%)
<b>Smoking history</b>	
Not known	7 (20 %)
non smoker	15 (42.9%)
Smoker	13 (37.1%)
<b>Pathology</b>	
Large cell carcinoma	2 (5.7%)
Adenocarcinoma	22 (62.9%)
Squamous cell carcinoma	8 (22.9%)
Mucoepidermoid carcinoma	1 (2.8%)
Bronchoalveolar carcinoma	2 (5.7%)
<b>Grade</b>	
Not known	6 (17.1%)
Low grade	2 (5.7%)
Intermediate grade	11 (31.4%)
High grade	16 (45.7%)
<b>Stage</b>	
II B	2 (5.7%)
III A	19 (54.3%)
III B	14 (40%)

**Table 2:** Response rate.

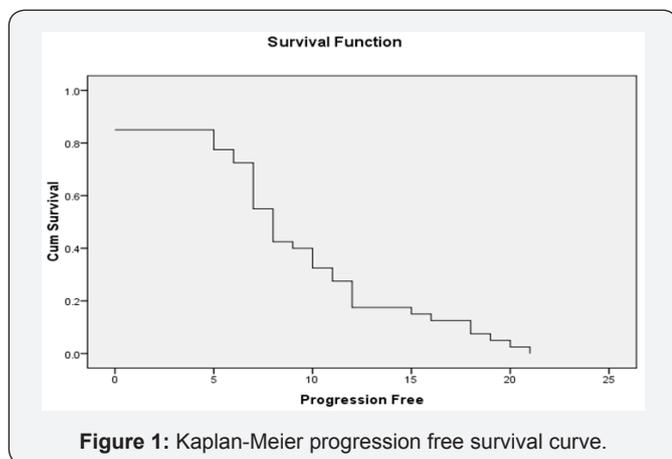
Response	N=35 No. (%)
CR	1 (3%)
PR	18 (51.5 %)
SD	12 (34%)
Progression	4 (11.5%)

Between January 2008 and December 2013, thirty five patients with newly diagnosed, non- metastatic NSCLC were included for this analysis. Patient’s characteristics and tumors features were mentioned in Table 1. As regard response rate only one patient (3%) achieved complete response (CR), partial response (PR) was detected in 18 patients (51.5%), stationary disease (SD) was demonstrated in 12 patients (34 %) and 4

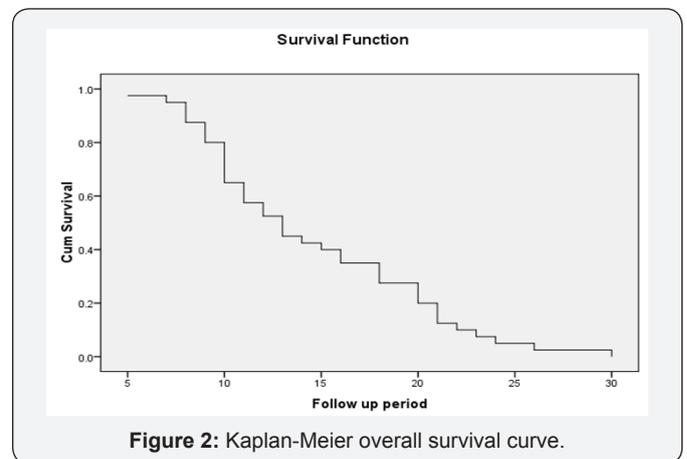
patients (11.5%) had progressive disease as summarized in Table 2. The most common toxicity was the hematological toxicity. Leucopenia was detected in 5 patients (14%); (grade I was 5.7 %), (grade II was 5.7 %), and (grade III was 2.8 %). Thrombocytopenia was found only in one patient (2.8%) and was grade I. Three patients (8.5%) developed anemia during therapy, 2 patients (5.7 %) was grade I anemia and 1 patient (2.8%) was grade II. Other adverse effects as peripheral neuropathy was observed in 3 patients (8.5%), grade I was in one patient and grade II was detected in 2 patients (5.7 %). Two patients (5.7 %) suffered from grade II emesis. Also diarrhea was noticed in 2 patients (5.7 %). Less common toxicities were observed as rising serum creatinine as shown in Table 3. Survival analysis was done for this study showed that median PFS was 8 months (95% Confidence Interval, 6.774 -9.226 months) as shown in Figure 1. The median OS was 13 months (95% Confidence Interval, 10.533 -15.467 months) as shown in Figure 2.

**Table 3:** Treatment toxicities.

Types	Total	N=35					
		Grade 1		Grade 2		Grade 3	
		No.	%	No.	%	No.	%
Leucopenia	5	2	5.7	2	5.7	1	2.8
Thrombocytopenia	1	1	2.8	0	-	0	-
Anemia	3	2	5.7	1	2.8	0	-
Peripheral neuropathy	3	1	2.8	2	5.7	0	-
Emesis	2	0	-	2	5.7	0	-
Diarrhea	2	1	2.8	1	2.8	0	-
Rising serum creatinine	1	1	2.8	0	-	0	-



**Figure 1:** Kaplan-Meier progression free survival curve.



**Figure 2:** Kaplan-Meier overall survival curve.

## Discussion

Our study was a retrospective study included 35 patients with non-metastatic NSCLC received taxol based chemotherapy. It showed male predominance 57% and female percentage was 43% in comparable to the study of Liao WY et al. [8] at 2013 with male 52% and female percentage 48% Liao et al. [8]. In our study 94 % of patients had stage III disease. Complete response (CR) was achieved in one patient (3%) and 20 patient (51.5 %) showed partial response (PR) with overall response rate (ORR) (54.5%) , while Kocher F and his colleagues at 2014 evaluated response after induction of docetaxel and cisplatin in 78 chemo-naïve patients with NSCLC stage II, IIIA and IIIB. Partial response to induction therapy was observed in 43 patients (55%) Kocher et al. [9]. Liao WY and his colleagues at 2013 demonstrated the efficacy of taxanes among 62 patients with stage III N2 NSCLC, CR was detected in one patient (2%) and PR was achieved in 25 patients (40%) with ORR (42%) Liao et al. [8]. Other studies as Chen YM et al. [10], Stathopoulos GP et al. [11], Inoue A et al. [12] showed ORR 40%, 42.86%, 45% respectively. This difference could be attributed to larger sample size in other studies.

The median OS in our study was 13 months (95% Confidence Interval, 10.533 -15.467 months) which cope with Bonomi P et al. [13] results. Their study included 599 patients to Compare OS and life quality in advanced non-small-cell lung cancer patients treated paclitaxel combined with cisplatin versus etoposide with cisplatin. The median survival duration for the stage IIIB subgroup in paclitaxel arm was 13.1 months. A randomized phase II study compare weekly paclitaxel versus vinorelbine in combination with cisplatin against inoperable chemo-naïve non-small-cell lung cancer included 140 patients.

The median survival time was 11.7 months in the paclitaxel-cisplatin arm Y Chen et al. [14]. Also the results obtained in our series are better than Fossella F et al. [15], Sandler A et al. [16], Lynch TJ et al. [17] and Zhu J et al. [18] with OS 11.3, 10.3, 8.38 , 8.9 months respectively. This difference could be attributed to larger sample size in these studies; also these studies included stage III and IV disease, so their OS lower than the OS in our study. Regarding PFS in our study was 8 months and were higher than Chen YM et al. [10], Mok TS et al. [19], Mitsudomi T et al. [20] and Niho S et al. [21] that reported median PFS of 6, 5.8, 6.3, 5.9 months respectively.

The commonest toxicity in our study was the hematological toxicity. Other adverse effects as peripheral neuropathy was observed in 3 patients (7.5%), 2 patients (5%) suffered from grade II emesis and diarrhea was noticed in 2 patients (5%) only. On the other hand; Kosmidis P et al. [22] demonstrated mild toxicities in paclitaxel and carboplatin combinations for the treatment of advanced non-small-cell lung cancer. Grades 3/4 neutropenia, thrombocytopenia, and anemia were seen in (15%) and (15%), (2%) respectively Kosmidis et al. [22]. Inoue A et al. [12] assessed toxicities of weekly paclitaxel combined with carboplatin in elderly patients with advanced NSCLC.

The most Common toxicities were hematological; Grades 3/4 leucopenia, thrombocytopenia, and anemia were observed in (30%), (15%), (13%) respectively, while peripheral neuropathy and nausea were detected only in 3% of patients. The higher hematological toxicities in this study could be explained by the old age that may be liable for more adverse events Inoue et al. [12]. Scagliotti GV and his colleagues reported at 2010 the adverse effects of carboplatin and paclitaxel in chemotherapy-naïve patients with advanced NSCLC. Neutropenia was 7%, thrombocytopenia was 3%, Anemia was 9%, peripheral neuropathy was 13%, vomiting was 7%, diarrhea was 13 % and oral mucositis was 2% Scagliotti et al. [23].

## Conclusion

In conclusion in our study; taxol are active class of chemotherapeutic agents in NSCLC and well tolerated. This agent exhibit clinical differences that can affect the choice of agents. However, further studies with longer follow up are needed for better orientation and comparisons with other agents.

## Disclosure

The authors have no conflicts of interest to disclose.

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