DOI: 10.38103/jcmhch.86.10

Original research

THE EFFICACY OF FIRST LINE PACLITAXEL - CARBOPLATIN WITH ADVANCED NON - SMALL CELL LUNG CANCER

Tran Anh Thuy Duong[1], Pham Nguyen Tuong[2]
[1]Ho Chi Minh City Oncology Hospital
[2]Oncology Center, Hue Central Hospital

ABSTRACT

Objective: *The aim of this study was to evaluate the outcomes of initial Paclitaxel - Carboplatin (TC) treatment in patients with advanced non - small cell lung cancer.*

Methods: *A total of 38 patients diagnosed with de novo NSCLC stage from IIIB to IV were underwent TC regimen from 2 to 6 cycles between February 2021 and July 2022 at Hue university of medicine and pharmacy hospital and Hue central hospital. They were assessed the response, progression - free survival, overall survival, and toxicity.*

Results: *The mean age was 58.4 ± 6.7. All patients had ECOG scores of 0 and 1. There was 18.4% cases with underweight. The figure for stage IV and non - squamous cell carcinoma (non - SCC) were 86.8% and 84.2%, respectively. 44.7% of patients received Pegfilgrastim. The improvement of cough, chest pain and dyspnea occurred after the first 6 weeks and maintained stable these symptoms until the 12th week. The object response rate (ORR) was 31.6%. The median progress - free survival and overall survival were 7.0 months and 14.0 months, in turn. Adverse events (AEs) at grades 3 or 4 presented 10.6% and 5.2% of patients with neutropenia and anemia. Hepatitis and renal impairment were less common.*

Conclusion: *In patients with previously untreated advanced non - small cell lung cancer, Paclitaxel - Carboplatin not only had efficacy and safety with an acceptable toxicity profile but also reduced the specific symptoms.*

Keywords: *Non - small cell lung cancer, advanced stage, Paclitaxel - Carboplatin.*

Received:
01/5/2022
Revised:
03/6/2023
Accepted:
04/6/2023
Corresponding author:
Pham Nguyen Tuong
Email: phamnguyentuong ubhue@gmail.com
Phone: 0913493432

I. INTRODUCTION

Non - small cell lung cancer (NSCLC) is a common malignant disease. The majority of patients present with advanced stage at the time of diagnosis. Although, the first treatment methods such as targeted therapy and immunotherapy demonstrate the outweigh in terms of response rate, survival and safety, platinum doublet - based chemotherapies to this day, are the cornerstone that are globally use, indicating patients with gene (EGFR, ALK…) mutation - negative or PD - L1 negative NSCLC, and those are not able to approach optimal treatments [1, 2]. Among these, Paclitaxel - carboplatin illustrates the similarity of efficacy with about 30% objective response rate, approximately 12 months of the median overall survival (OS) and the acceptable toxicity, the safety for 60 - year - old patients, and the alleviaton of symptoms [3, 4]. At Hue central hospital and Hue University hospital, this regimen is one of the popular options. Therefore, our objective was to evaluate the results of the first - line TC treatment with advanced NSCLC.

II. MATERIALS AND METHODS

2.1. Patients

All 38 patients entered onto this study were 18 years of age or older and diagnosed de novo NSCLC with stage IIIB, IIIC, and IV according

to TNM8 of the American Joint Commission on Cancer, confirmed by pathology with or without immunohistochemistry test. Those with an Eastern Cooperative Oncology Group (ECOG) performance - status score of 0, 1 or 2 received paclitaxel 175 - 200 mg/m^2 and carboplatin with area under the concentration - time curve of 4 - 5 mg/mL/min (range, 2 to 6 cycles), each administered every 3 weeks. The study excluded the patient with uncontrolled brain metastasis. We conducted from February 2021 to July 2022.

2.2. Methods

In this descriptive study, patients were assessed symptoms per the EORTC QLQ - LC13 questionnair before the first day of cycle 1, after 6 and 12 weeks, and responses per the Response Evaluation Criteria in Solid Tumors (RECIST) ver 1.1. Toxicity was performed in accordance with the National Cancer Institute common toxicity criteria (CTCAE) version 5.0. Kaplan - Meier method was used to estimate progress - free survival and overall survival. The log - rank test analysed the relevant factors. The Cox regression model was used for the multivariate analysis of significant survival variables from the Kaplan - Meier method. Paired - T test was used to compare 2 mean scores of a measurement at two assessed times. Statistical significance was determined at $p < 0.05$.

All statistical analyses were performed with SPSS software version 16.

III. RESULTS

3.1. Clinical and laboratory patient characteristics

This study included 38 eligible patients with a mean age 58.4 ± 6.7 (39 - 70). After 6 weeks, there were 2 patients who died before reaching the 12th week.

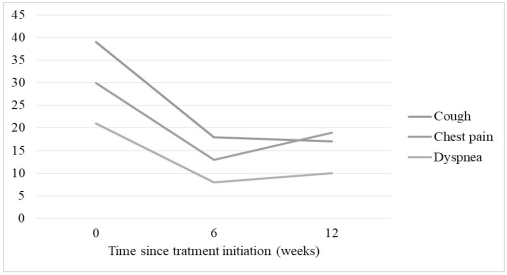
Table 1: Patient characteristics

Characteristic		n	%
Sex	Male	29	76.3
	Female	9	23.7
Body mass index (BMI) kg/m^2	< 18.5	7	18.4
	≥ 18.5	31	81.6
ECOG performance status	0	3	7.9
	1	35	92.1
	2	0	0
Histologic subgroup	Non - SCC	32	84.2
	SCC	6	15.8
EGFR mutation test	Positive	3	7.9
	Negative	10	26.3
	Not given	33	65.8
Metastases	No	5	13.2
	Yes	33	86.8

Characteristic		n	%
Distant metastatic sites	Contralateral lung	8	21.1
	Pleura	20	52.6
	Bone	14	36.8
	Adrenal gland	5	13.2
	Brain	2	5.3
	Liver	2	5.3
Controlled brain metastases	Whole brain radiotherapy	1	2.6
	Surgery	1	2.6
The use of Pegfilgrastim	Yes	17	44.7
	No	21	55.3

The rate of male/female was 3.2/1 and 18.4% of patients were underweight. All they had ECOG scores of range 0 to 1. Only 34.2% of patients were performed EGFR mutation test. Those with stage IV were predominant (86.8%) including 2 patients who underwent controlled brain metastases before undergoing chemotherapy. 44.7% of patients received Pegfilgrastim.

3.2. Efficacy



The scores of cough, dyspnea, and chest pain decrease 6 weeks later ($p < 0.05$). At the 12th week, these levels were almost unchangeable (cough, dyspnea) and less changeable (chest pain), as compared with the 6th week levels ($p > 0.05$).

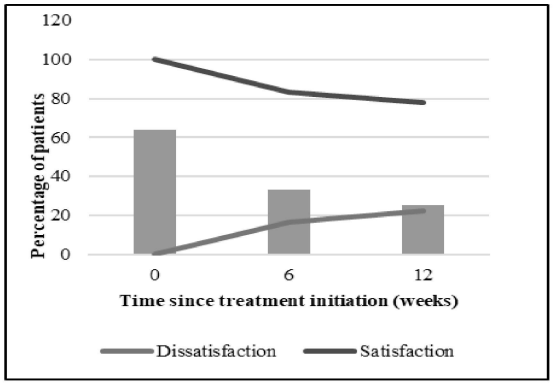


Chart 2: The rate of patients receiving analgesics and their satisfaction with the alleviate

The number of patients using analgesics decreased moderately from time to time. In the 6th and 12th weeks, 2 patients were still unpleasant about the efficacy of drugs.

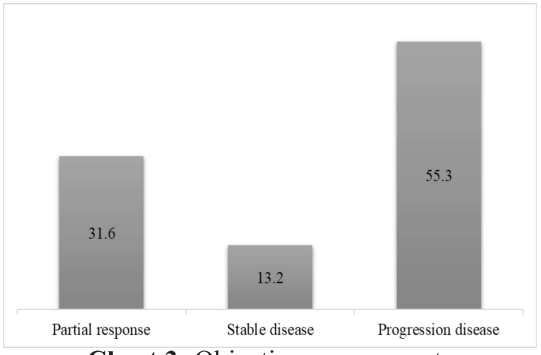


Chart 3: Objective response rate

No patient was attained completed response.

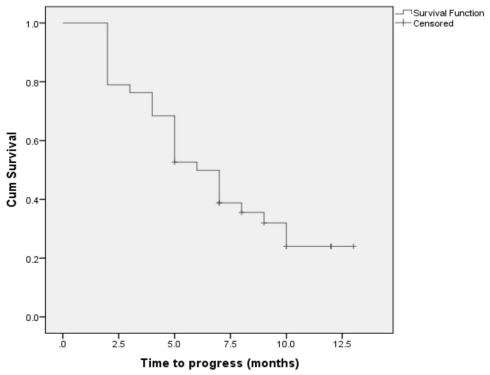


Chart 4 : Progression - free survival

Median PFS was 6.0 ± 0.8 months (95% CI: 5.7 - 8.4)

Table 2: Factors influencing PFS identified by Log - rank test and Cox regression analysis

Sinh thiết					Sinh thiết			
Characteristics		**Time (month)**	**SD**	**p**	**Hazar Ratio**	**95% CI**		**p**
Sex	Male	7.0	0.8	0.776	1			0.991
	Female	6.6	1.4		0.99	0.358	2.762	
BMI	<18.5	3.4	0.8	0.001	1			0.011
	≥18.5	7.9	0.7		0.27	0.100	0.741	
ECOG	0	5.7	0.5	0.994	1			0.702
	1	7.0	0.7		1.35	0.293	6.180	
Metastasis	M0	8.8	1.4	0.275	1			0.583
	M1	6.7	0.7		1.45	0.386	5.428	
Histology	Non - SCC	7.1	0.7	0.638	1			0.615
	SCC	5.4	0.9		1.35	0.422	4.306	

PFS of underweight group was 3.4 months, lower than those without underweight (7.9 months). Also underweight was a prognostic factor influencing PFS.

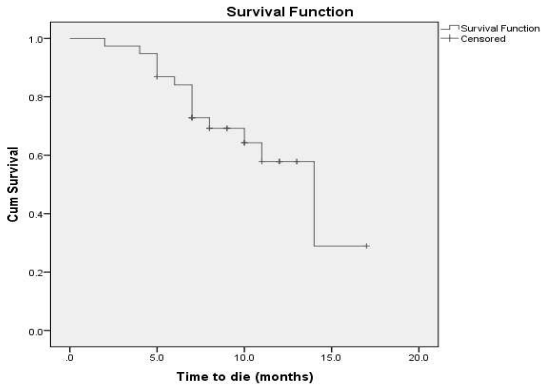


Chart 5. Overall survival

Median OS was 14 ± 2 months (95% CI: 10 - 14)

3.3. Safety

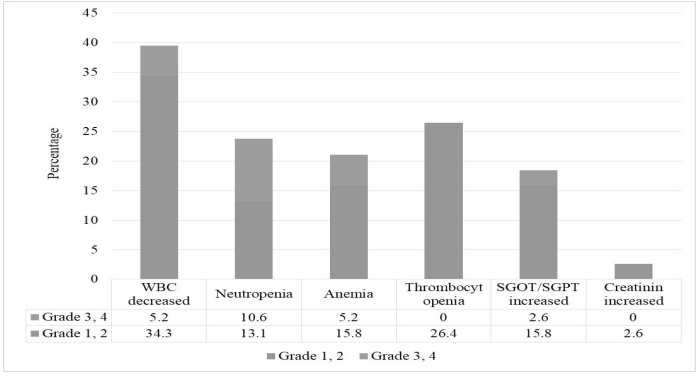


Chart 6: Hematological toxicity, hepatic and renal adverse events.

The adverse event of grade 5 didnot observe. 10.6% of patients were reported to have neutropenia of grade 3 or 4. A patient developed transaminase elevation with grade 3.

Table 3: Nonhematological toxicity (n = 38)

Adverse Events	No event		Grade 1, 2	
	n	%	n	%
Allergy	38	100	0	0
Nausea/vomiting	25	65.8	14	34.3
Alopecia	0	0	38	100
Peripheral neuropathy	23	60.5	15	39.5
Arrhythmia	28	73.7	10	26.3

No case occurred grades 3-5 of the toxicity.

IV. DISCUSSION

A total of 38 eligible patients treated with first - line paclitaxel - carboplatin were 58.4 ± 6.7 mean age and had ECOG 0 - 1. In clinical practice, patients old or having ECOG scores > 2 often less consider multi - drugs chemotherapy, immunotherapy, might be allowed to take TKIs, monotherapy, or palliative care. TKIs could apply the patients with high - grade ECOG or the old [2]. A certain number of patients in our study were not approached EGFR mutation test as well as the panel gene. Only 26.3% of patients were confirmed EGFR mutation negative and 66% of those were not given information. The number of patients using Pegfilgrastim was 44.7% including 23.7% of them were used for secondary prevention and the rest aimed to prevent from neutropenia during Covid pandemic.

Several researches in the world and in Viet Nam such as Avelino or Phung Phuong's studies showed the result as same as us in terms of the improvement of cough, dyspnea, and chest pain 6 weeks later ($p < 0.05$). In the 12th week, they were nearly stable [5, 6]. Moreover, beyond chest pain, our patients suffered from other pain sites (bone, head, huge cervical lymph nodes, legs). The combination between chemotherapy and palliative care allowed a decrease in the use of analgesics over time. However, 2 patients had consistent pain and were dissatisfied because of the progression disease, severe bone metastasis, and breakthrough pain sometimes.

Table 4 : Objective response rate in some studies

Author	ORR (%)
Vu Hong Thang (2013) [3]	31.7
Hosein Borghaei et al (2020) [7]	29.8
KEYNOTE - 021 with Pemetrexed - Carboplatin arm [1]	33
Masato Komuro (2015) [8]	32.4
Our study	31.6

The objective response in our study was quite the same rate as several study reports regarding TC and other doublet chemotherapies (around 30 - 40%).

The median PFS and OS were 7 months and 14 months, respectively, which was similar to the results of Han Thi Thanh Binh, Kumuro, and KEYNOTE - 047. Moreover, Komuro reported that Asian region was found to be a prognostic factor that affects longer OS in treatment with TC as first - line chemotherapy [8 - 10]. However, the authors found better OS outcomes in patients treated with pemetrexed - based chemotherapies with non - squamous cell carcinoma [11]. Findings of prognostic factors affecting PFS were different among the studies, while we identified underweight as a factor affecting higher progression disease, the other findings showed stage, and histologic types factors [8, 10].

The notable drug - related adverse event was hematological toxicity, especially neutropenia. The neutropenia grades 3 - 5 rates were 10.6% in our report, 24.6% in KEYNOTE - 047 trial or higher

when using cisplatin - based chemotherapies. The lower rate in our finding might result in 44.7% of patients receiving Pegfilgrastim. Anemia and thrombocytopenia were observed grade 1 or 2, with around 20%. Hepatitis and renal impairment were less common (< 10%). Alopecia, nausea/vomiting, peripheral neuropathy, and arrhythmia occurred frequently (> 10%) [10].

V. CONCLUSION

The efficacy benefits of paclitaxel - carboplatin were seen to alleviate several specific symptoms related - disease after the first 6 weeks, with 31.6% of objective response rate and modest survival improvement. The toxicity profile was acceptable and might be prevented by supportive care.

REFERENCE

1. Awad MM, Gadgeel SM, Borghaei H, Patnaik A, Yang JC, Powell SF, et al. Long-Term Overall Survival From KEYNOTE-021 Cohort G: Pemetrexed and Carboplatin With or Without Pembrolizumab as First-Line Therapy for Advanced Nonsquamous NSCLC. J Thorac Oncol. 2021;16(1):162-168.
2. Sakata Y, Sakata S, Oya Y, Tamiya M, Suzuki H, Shibaki R, et al. Osimertinib as first - line treatment for advanced epidermal growth factor receptor mutation - positive non - small - cell lung cancer in a real - world setting (OSI-FACT). Eur J Cancer. 2021;159144-153.
3. Đường Lê Thế, Vũ Hồng Thăng. Đánh giá đáp ứng của phác đồ paclitaxel - carboplatin trên nhóm bệnh nhân trên 60 tuổi. Tạp chí ung thư học Việt Nam. 2013168-173.
4. Mok TSK, Wu Y - L, Kudaba I, Kowalski DM, Cho BC, Turna HZ, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non - small - cell lung cancer (KEYNOTE - 042): a randomised, open - label, controlled, phase 3 trial. The Lancet. 2019;393(10183):1819-1830.
5. Avelino CU, Cardoso RM, Aguiar SS, Silva MJ. Assessment of quality of life in patients with advanced non-small cell lung carcinoma treated with a combination of carboplatin and paclitaxel. J Bras Pneumol. 2015;41(2):133-42.
6. Chuyên NTH. Khảo sát chất lượng sống ở bệnh nhân ung thư phổi tiến xa được hóa trị triệu chứng. Luận văn thạc sĩ y học. 2015.
7. Borghaei H, Langer CJ, Paz-Ares L, Rodriguez-Abreu D, Halmos B, Garassino MC, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone in patients with advanced non-small cell lung cancer without tumor PD-L1 expression: A pooled analysis of 3 randomized controlled trials. Cancer. 2020;126(22):4867-4877.
8. Komuro M, Kaneko M, Narukawa M. Investigation of prognostic factors affecting efficacy in carboplatin - and paclitaxel - based first - line chemotherapies for advanced non - small - cell lung cancer. Tumori. 2015;101(4):424-32.
9. Paz - Ares L, Luft A, Vicente D, Tafreshi A, Gumus M, Mazieres J, et al. Pembrolizumab plus Chemotherapy for Squamous Non - Small - Cell Lung Cancer. N Engl J Med. 2018;379(21):2040-2051.
10. Bình HTT. Nghiên cứu điều trị ung thư phổi không tế bào nhỏ giai đoạn IIIB, IV bằng hóa trị phác đồ cisplatin kết hợp với paclitaxel hoặc etoposide. Luận văn tiến sĩ Y học, Trường Đại học Y Hà Nội. 2018.
11. Liu M, Luo N, Fang Z, Liu Q, Yi F, Wei Y, et al. The efficacy and toxicity of maintenance therapy with bevacizumab plus pemetrexed versus bevacizumab/pemetrexed alone for stage IIIB/IV nonsquamous non-small cell lung cancer: A meta-analysis of randomized controlled trials. J Clin Pharm Ther. 2022;47(2):157-167.