VINORELBINE AS SECOND-LINE TREATMENT OF NSCLC AFTER THE FAILURE OF PLATINUM-TAXANE COMBINATION AT THE HUE UNIVERSITY HOSPITAL

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ABSTRACT

Lung cancer is the most prevalent malignancy and the leading death caused by cancer worldwide. It is also the most common cancer in Vietnam. With the high prevalence and high mortality rate, lung cancer is the real burden of healthcare today. NSCLC accounts for about 85-90% of lung cancer. Lung cancer is mostly diagnosed at a late stage that the goal of the treatment is palliative. The advent of new targeted therapies for NSCLC is making a huge change in the practice of lung cancer treatment. But due to lacking resources, chemotherapy is still playing an important role in Vietnam. After the first-line chemotherapy, patients degrades a lot and it raises the question of choosing an appropriate drug for the continuous treatment. Vinorelbine was found to be effective in NSCLC treatment and it was introduced in Vietnam in 2006. Some studies showed its efficacy in treating NSCLC at a late stage of the first line in Vietnam but lacking information on vinorelbine application for second-line treatment.

***Methods**: A retrospective cohort study of 32 patients with NSCLC staged IIIB-IV treated by vinorelbine as second-line after the failure of Paclitaxel and carboplatin combination for the first-line at the Hue University hospital from 2013-2017. Vinorelbine was administered on day 1, day 8 and day 21.*

Statistical analysis was performed in R program.

***Results:** Our study composed of a higher rate of squamous cell carcinoma (43.75%) versus adenocarcinoma (28.12%). 78.13% were at stage IV. The most common metastatic sites were lung, pleura, and bone. The response rate was 28.13%. No cases of complete response were observed. Symptoms were improved in 19 patients (59.34%). The median of OS was 41 weeks. Anemia, neutropenia, and nausea were the most frequently observed in only one case of grade IV anemia.*

***Conclusion**: Vinorelbine was found to be effective with high tolerability as a second-line treatment for NSCLC at stage IIIB-IV.*

***Keywords:** NSCLC, lung cancer, vinorelbine, second-line.*

I. INTRODUCTION

Lung cancer is the most prevalent malignancy with 1.8 million newly diagnosed cases in 2012 and the leading death caused by cancer with about 1.59 million died of this cancer worldwide. It is also the most common cancer in Vietnam with high mortality [1], [2], [3], [4] thus enabling behavior to vary adaptively from moment to moment.

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Dominating contemporary research on this topic is the viewpoint that self-control relies upon a limited resource, such that engaging in acts of restraint depletes this inner capacity and undermines subsequent attempts at control (i.e., ego depletion. With the high prevalence and high mortality rate, lung cancer is the real burden of healthcare today for every country.

Lung cancer is composed of small cell lung cancer and non-small cell lung cancer (NSCLC). In which, NSCLC accounts for about 85-90% of lung cancer [4]. Lung cancer is mostly diagnosed at a late stage that the goal of the treatment is palliative. The advent of new targeted therapies for NSCLC is making a huge change in the practice of lung cancer treatment [1], [4]. But due to lacking resources, chemotherapy is still playing an important role in Vietnam, especially in central Vietnam where local people are still poor. A doublet of platinum-based regimen is usually indicated for patients with NSCLC staged IIIB-IV whose general status OMS was 0-2. Taxane and carboplatin regimen is widely used for the first line of the treatment with comparable efficacy to other chemotherapy combinations and acceptable toxicities. After the failure of this first-line treatment, patients normally degrades a lot and it raises the question of how to choose an appropriate chemotherapy. For second-line chemotherapy, monotherapy is preferred and among many third generation drugs, docetaxel was found to have higher efficacy in comparison to others chemotherapy drugs but the toxicities are more serious. [4], [5], [6].

Vinorelbine has been introduced in Vietnam since 2006. Some studies examined the combination of vinorelbine + platinum in treating NSCLC stage IIIB-IV for the first-line. These studies showed that vinorelbine in combination with platinum had the good outcome and fewer toxicities [7], [8]. But lacking studies of vinorelbine monotherapy after the failure of platinum doublet especially taxane and carboplatin. The application of vinorelbine in Hue in recent years without known report to the authors. So, we conducted the study "vinorelbine as second-line treatment of NSCLC after the failure of the platinum-taxane combination at the Hue University hospital" with aims:

- To describe the characteristics of NSCLC at late stage treated at the Hue University hospital with vinorelbine as the second-line treatment after the failure of carboplatin and taxane regimen.
- To reveal the efficacy of vinorelbine as a second-line monotherapy.
- To depict the toxicities of vinorelbine.

II. PATIENTS AND METHODS

A retrospective cohort study of 32 patients with NSCLC staged IIIB-IV treated with vinorelbine after the failure of the Paclitaxel and carboplatin regimen for the first line at the Hue University hospital from 2013-2017. Vinorelbine was administered on day1-8 every 21 days, at least 3 cycles of the treatment. Vinorelbine day 1 at 25-30 mg/m^2 IV, Vinorelbine day 8 at 60-80 mg/m^2 day 8. We excluded those cases that lack needed information.

We measured overall survival from the time of treating vinorelbine till death or last follow up if patients are still alive. The response of the chemotherapy was evaluated by RECIST criteria. Statistical analysis was performed by R program.

III. RESULTS

3.1 Description of the subjects

In our study group, the mean age was 58 years old with a range from 45-79. The male/female ratio was 1.67: 1. Pathologically, the squamous cell carcinoma was much higher than adenocarcinoma (43.75% vs 28.12%). Patients were majorly at stage IV with the percentage of 78.13% (Table 1).

Pleura, lungs and bone were among the most common sites of metastasis (Table 2, 3)

Table 1. Some common characteristics of the study group

Characteristics		n	%
Gender	male	20	62.5%
	female	12	37.5%
Affected lung	left	17	53.13
	right	15	46.87
Pathology	squamous	14	43.75
	adenocarcinoma	9	28.12
	mixte	1	3.13
	large cell	2	6.25
	unknown type	6	18.75
Stage of cancer	stage IIIB	7	21.87
	stage IV	25	78.13

In the study group, male patients were more prevalent than women, squamous cell carcinoma was found dominantly and patients were almost metastatic with stage IV of 78.13%.

Table 2. Metastatic sites at the time of diagnosis

Site of metastasis	**n**	**%**
liver	2	7.41
pleura	14	51.85
pericardium	2	7.41
lungs	11	40.74
bone	10	37.04
kidney	1	3.70
brain	1	3.70

Table 3. Metastatic sites before vinorelbine

Metastatic sites before vinorelbine	**n**	**%**
Liver	4	12.5
Pleura	15	46.88
Brain	3	9.38
Lungs	16	50.00
Adrenal glands	1	3.13
Bone	13	40.63

The most common metastatic sites at the time of diagnosis and before treating vinorelbine were lungs, pleura, bone, brain in order of high to low prevalence.

3.2 The outcome of the treatment

After 3 cycles of chemotherapy, 18 cases were found to have progression of the disease, 9 cases were partially responded and 5 were stable. The response rate was 28.13%. There were no cases of complete response.

About the clinical response, symptoms were observed to be improved after 3 cycles of vinorelbine in 19 patients (59.34%).

The survival analysis showed that the median of OS was about 41 weeks (about 10 months) and the survival rate was higher in patients with stage IIIB (p=0.45). (Figure 1).

Table 4. Response rate of vinorelbine

Response	**n**	**%**
Complete response	0	0
Partial response	9	28.12
Stable disease	5	15.63
Progression	18	56.25

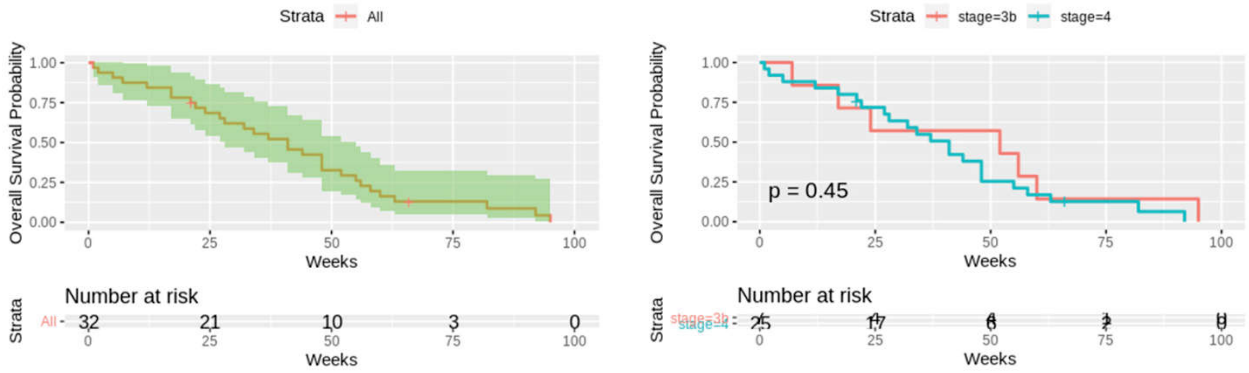

Figure 1. Overall survival analysis

3.3. Toxicities of vinorelbine

Most toxicities were grade 1-2. Anemia, neutropenia, and nausea were the most frequently observed toxicities in patients treated with vinorelbine. The rate of patients got anemia, neutropenia and nausea at all grades were 31.25%, 21.88% and 25% respectively. One patient had anemia grade 4 (Table 4).

Table 4. Toxicities of Vinorelbine

Toxicity	All grades	Grade 3-4
Hematological		
Thrombocytopenia	1 (3.13%)	0
Neutropenia	7 (21.88%)	0
Anemia	10 (31.25%)	1 (3.13%)
Non-hematological		
Nausea	8 (25%)	0
Vomitting	2 (6.25%)	0
Diarrhea	3 (9.38%)	0
Sensorial neuropathy	3 (9.38%)	0
Mucositis	1(3.13%)	0
Extravasation	2 (6.25%)	0

IV. DISCUSSION

From our cohort of 32 patients with NSCLC stage IIIB-IV. The mean age was 58 years old. The youngest patient was 45 and the oldest was 79. The male/female ratio was 1.67: 1. These are rather similar to some studied cohorts in the north of Vietnam [8], [9]. The rate of adenocarcinoma in our study was lower to other authors [8], [9] [10]. This may due to the high rate of unknown types in our study. More elective studies with the exclusion of cytology confirmation may explain this difference more clearly.

The most common metastatic sites were pleura, lungs, and bone. This is well known in the literature of lung cancer.

In term of the efficacy of Vinorelbine, the response rate was 28.13% which is higher than the rate from the western countries [5] but rather similar to the author Le Chinh Dai at the K hospital [9]. This rate of response rate was lower than the author Nguyen Huu Khiem in which, the response rate was 33.5% and 35.1% for stage IIIB and IV. These differences may come from the difference in pathology, the previous treatment.

A good clinical response was observed at 59.34%. And the median OS was 41 weeks. These findings are really promising for NSCLC at a late stage after the failure of the first-line therapy.

Moreover, toxicities profiles were not severe. Most toxicities were at grade 1-2 and only one grade 4 of anemia was observed and easily managed by transfusion. Many international and local studies of vinorelbine also found the same remark that vinorelbine is tolerable to NSCLC patients and the grade 3-4 toxicities are minimal. [8], [9], [11] excluding non-melanoma skin cancer. Non-small cell lung cancer (NSCLC

Our findings showed that vinorelbine could be another option for NSCLC which progresses after the first line of platinum-taxane. Though many targeted therapies and other chemotherapies were proved to be effective, the low cost and less toxicity of vinorelbine make it reasonable to indicate in treating NSCLC. A larger and prospective study is needed to confirm our findings.

V. CONCLUSION

Vinorelbine was found to be effective with high tolerability as a second-line treatment for NSCLC at stage IIIB-IV. The result needs a well structured larger prospective study to confirm for more conclusive findings.

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