Original Research

# EVALUATING THE TREATMENT RESULTS OF VINORELBINE MONOTHERAPY IN NON-SMALL CELL LUNG CANCER

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**ABSTRACT**

***Objective:*** *Vinorelbine monotherapy has been shown to be effective in recurrent or metastatic non-small cell lung cancer. This study aimed at evaluating the treatment results of vinorelbine monotherapy in lung cancer patients relapsed after curative treatment.*

***Patients and methods****: Descriptive study of 56 non-small cell lung cancer patients who were treated with vinorelbine monotherapy relapsed after curative treatment at National Cancer Hospital between June 2018 and August 2020.*

***Results:*** *The mean age was 56.9 years old. Ratio male:female = 3.3:1. The percentage of adenocarcinoma and squamous cell carcinoma was 67.9% and 26.8%, respectively. Most patients (76.8%) relapsed within one year after curative treatment. The most common relapse sites were lung, bone, and pleura (85.7%, 33.9%, 30.4% respectively).The total number of treatment cycles was 428 with the average number of cycles was 6.1 ± 3.2, ranging from 2 to 21 cycles. Treatment response: no patient achieved complete response, the disease control rate was 76.8% (partial response rate 21.4%, the stable disease rate 55.4%). Histopathology and the number of relapsed site did not affect the response rate. Median PFS was 5.3 months. The number of cycles of leukopenia and neutropenia accounted for 32.5% and 34.1%, respectively, of which only 1.4% was in grade 3 and grade 4. Other common nonhematologic side effects were nausea/vomiting (15.2%); diarrhea (4.7%) and gastritis (2.8%), which were mild and did not affect the treatment course.*

***Conclusion:*** *Vinorelbine monotherapy is an effective option in relapsed NSCLC patients with a good safety profile.*

***Keywords:*** *Lung cancer, vinorelbine monotherapy, NSCLC, recurrence*

## I. INTRODUCTION

According to GLOBOCAN 2020, lung cancer was the most common malignancy in many countries around the world [1]. In Vietnam, lung cancer was the second most common disease in both sexes [2]. Around 35% of patients were initially diagnosed at locally advanced stage and then 80-85% of them

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developed recurrence. Recurrence also happened in 30-40% of patients with early stages, even after curative surgery [3]. For patients in the late stage, systemic therapy (chemotherapy, targeted therapy, and immunotherapy) is the optimal treatment for alleviating symptoms and extending quantity and quality of life [4].

Platinum-based combination chemotherapy has been widely used in patients with rapidly progressive disease and good performance status with aim to achieving maximum response. However, if the combination regimen fails, the monotherapy is preferred with the fewer side effects and better quality of life. Vinorelbine monotherapy has been shown to be effective in recurrent or metastatic lung cancer with response rate ranging from 8% to 37% [5-8], especially in elderly patients with poor performance status or severe comorbidities [9]. Currently at National Cancer Hospital, this regimen is also being used, but so far there have not been many studies on this topic. Therefore, we conducted this study named "Evaluating the treatment results of vinorelbine monotherapy in non-small cell lung cancer" with two objectives: "To evaluate the treatment results of vinorelbine monotherapy in non-small cell lung cancer" and "to" evaluate the adverse events of this regimen.

## II. PATIENTS AND METHODS

### Patients

We carried out a descriptive study in 56 patients with relapsed NSCLC treated with vinorelbine monotherapy at National Cancer Hospital from June 2018 to August 2020

Inclusion criteria were: (1) Stage I - IIIA NSCLC patients undergone radical surgery ± adjuvant chemotherapy or stage IIIB NSCLC patients with complete response after concurrent chemoradiation. AJCC 8th TNM staging system was used in this study. (2) Relapse setting diagnosed by cytology or histopathology. (3) Patients had no information about EGFR/ALK mutation or were unable to afford targeted therapy. (4) Patients had no information about PD-L1 status or were unable to afford immunotherapy. (5) Progression after platinum-based chemotherapy or had contraindication to platinum agents (Cisplatin, Carboplatin). (6) Have measurable target lesions for response evaluation (according to RECIST 1.0 criteria). (7) ECOG performance status ≤ 3. (8) Adequate liver and kidney function.

Exclusion criteria were: Brain metastasis; Hypersensitivity to vinorelbine; Patients dropped out not because of disease progression or adverse events; Patients received combination regimen with vinorelbine plus other anti cancer drugs.

### Treatment

Vinorelbine (30 mg per square meter of body-surface area) was administered intravenously over 6 to 10 minutes once a week. Treatment would be discontinued in case of disease progression, patient or clinician choice, or unacceptable toxic effects.

### Data collection

Patient characteristics: age, gender, clinicopathological characteristics, relapse sites, and histopathology. Number of vinorelbine cycles. Tumor response assessed after each 3 cycles. Progression free survival (PFS). Safety profile of vinorelbine (Hematologic toxic effects and nonhematologic toxic effects)

Data analyses were performed with the use of SPSS 16.0.

There is no institutional review board (IRB) at National Cancer Hospital (NCH). Therefore, the research was approved and supported by the Managing Council of NCH.

## III. RESULTS

### Treatment results

Mean age was 60.2 years old. The ratio of male:female was 3.3:1. 78.6% of all population developed recurrence within one year after finishing treatment. The most common recurrent sites were

lung, bone, and pleura (85.7%, 33.9%, 30.4% respectively). (**Figure 1**) These patients mainly presented with cough, chest tightness and dyspnea (71.4%, 50%, 33.9% respectively) (**Table 1**). 19.6% of all participants were asymptomatic. In terms of histopathology, adenocarcinoma accounted for the highest percentage (68%).

**Figure 1:** Sites of Recurrence

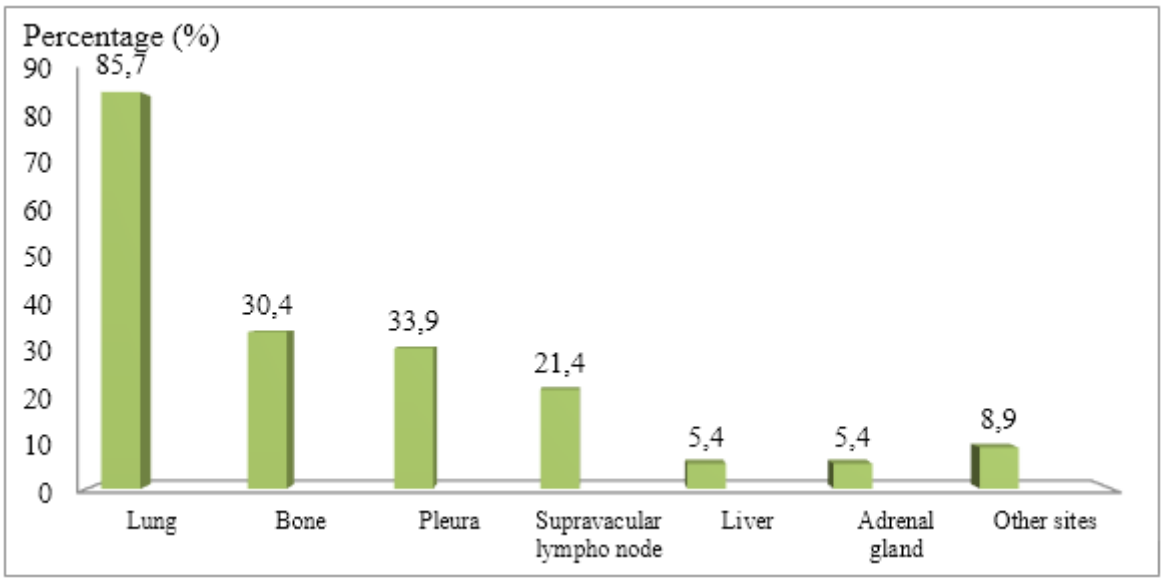


**Table 1:** Presenting symptoms

| Symptoms | Number of patients (n) | Percentage (%) |
|---|---|---|
| Cough | 40 | 71.4 |
| Chest pain | 28 | 50 |
| Dyspnea | 19 | 33.9 |
| Bone pain | 5 | 8.9 |
| Fever | 2 | 3.6 |
| Asymptomatic | 11 | 19.6 |

Most patients (88%) were treated with vinorelbine after one or two previous platinum-based chemotherapy regimens (51.8% and 35.7%, respectively). The total number of vinorelbine cycles in all population was 428. Mean vinorelbine cycles was 6.1 (ranging from 2 to 21 cycles). 91.1% of all patients received more than 85% of the standard dose. Symptoms such as cough, chest pain, and dyspnea were reduced during treatment, of which dyspnea improved most (57.9%), followed by chest pain (57.2%) and cough (52.5%). No patient achieved complete response. The disease control rate was 76.8% (partial response rate 21.4%, stable disease rate 55.4%). 23.2% of all participants progressed during study treatment. After 6 months, the progression free rate was 39.3%. 7 patients (12.5%) still had disease control after 12 months. (**Table 2**). There was no difference in response rates between adenocarcinoma subgroup and squamous cell carcinoma subgroup. Likewise, no difference was reported between solitary relapse and multiple-site relapse subgroups. Mean progression free survival (PFS) was 6.2 ± 3.8 months, and the median PFS was 5.3 months (**Figure 2**). 7 patients (12.5%) still had disease control after 12 months. (**Table 2**)

**Table 2:** Progression free survival

| | n | Rate (%) | Mean (months) | Median (months) |
|---|---|---|---|---|
| 6 months | 22 | 39.3 | 6.2±3.8 (Min=2 Max=21) | 5.3 |
| 9 months | 8 | 14.3 | | |
| 12 months | 7 | 12.5 | | |

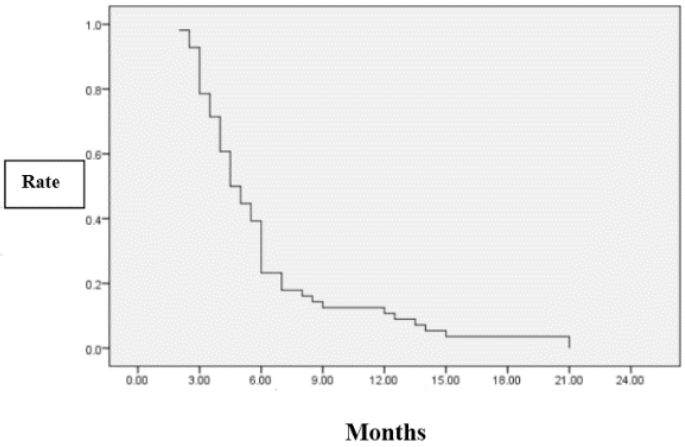


**Figure 2:** Progression free survival

**Safety profile of vinorelbine**

Hematologic toxic effects were the most common adverse events in this study. Of all 428 cycles, the leukopenia and neutropenia rates were 32.5% and 34.1%, respectively; mainly in grade 1 or 2 (**Table 3**). Rate of anemia was 30.4%, mostly in grade 1. Only 1.9% patients of all cycles developed thrombocytopenia.

**Table 3:** Neutropenia rates in correlation with the total number of cycles

| Number of cycles | Neutropenia (all grades) | | Grade 3/4 neutropenia | |
|---|---|---|---|---|
| | n | % | n | % |
| ≤ 3 | 24 | 16.4 | 0 | 0 |
| 4-6 | 53 | 36.3 | 3 | 50 |
| 7-9 | 37 | 25.3 | 2 | 33.3 |
| 10-12 | 21 | 14.5 | 1 | 16.7 |
| >12 | 11 | 7.5 | 0 | 0 |
| Total | 146 | 100 | 6 | 100 |

Most nonhematologic toxic effects were in gastrointestinal tract, manifested by nausea/vomiting (15.2%), diarrhea (7.5%) and gastritis (2.8%). Rate of liver enzyme increased was 20.8%, mainly in grade 1. Few patients developed renal dysfunction. None of all participants suffer from grade 3 and grade 4 liver or renal dysfuntion. (**Table 4**). Injection site reactions occur in about one-fourth of patients. All of them were tolerable with erythema and mild pain at injection site.

**Table 4:** Nonhematologic toxic effects / Total number of cycles

| Adverse events | Grade 0 | | Grade I | | Grade II | | Grade III | | Grade IV | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| Liver enzyme elevation | 339 | 79.2 | 78 | 18.2 | 11 | 2.6 | 0 | 0 | 0 | 0 |
| Creatinine level elevation | 423 | 98.8 | 5 | 1.2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Nausea/vomiting | 363 | 84.8 | 65 | 15.2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Gastritis | 416 | 97.1 | 12 | 2.8 | 0 | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 396 | 85.3 | 32 | 7.5 | 0 | 0 | 0 | 0 | 0 | 0 |

Most common adverse event rates were higher when using a dose more than 95% of the standard dose.

## IV. DISCUSSION

### Treatment results

Data of 56 patients was collected in this study. The male:female ratio was 3.3:1, which was similar to some recent studies [10-12]. The rate of adenocarcinoma and squamous cell carcinoma were 67.9%, and 26.8%, respectively. The rest were large cell carcinoma andadenos quamous carcinoma. This result was also similar to some studies of domestic and foreign authors [10,11,13].

Most patients in our study presented at stage II and III at the time of diagnosis, accounting for 94.6%. This result was higher than that of study of Shinsuke Saisho et al (2012) [13]. This could be explained by lacking of screening program in lung cancer in Vietnam [14,15]. The majority of patients (78.6%) were likely to develop distal recurrence in the first year after finishing treatment. This could also be observed in study of Shinsuke Saisho (2013) [13].

The total number of treatment cycles was 428 with the average number of cycles was 6.1 ± 3.2, ranging from 2 to 21 cycles. 69.7% of patients were treated with dose more than 95% of the standard dose. 17 patients had dose modification due to side effects during treatment, accounting for 30.3%. No patient had to discontinue treatment due to unacceptable side effects. Therefore, the side effects of vinorelbine monotherapy were mild and most patients were well tolerated. This could improve the efficacy of the regimen since treatment with the maximum dose would increase the inhibitory effect of the drug on cancer cells.

Cough, chest pain, and shortness of breath were the most common symptoms reported in our study. Rates of remission of these symptoms after treatment were 52.5%, 57.2% and 57.9%, respectively. Study of C. Gridelli et al (2001) on advanced lung cancer patients treated with vinorelbine also shown similar results (remission rate was around 64%) in three above-mentioned symptoms[9].

In our study, no patient achieved complete response. The partial response rate and the stable disease rate was 21.4% and 55.4%, respectively. 7 patients (12.5%) still had disease control after 12 months. Median PFS was 5.3 months. The results of our study were similar to the results of other studies around the world with the median of PFS ranging from 4 to 6 months [9,13].

### Safety profile of vinorelbine

The most common side effect of vinorelbine is the hematologic toxic effect. This could be

exemplified by analyzing the adverse events of all 428 cycles. The number of cycles of leukopenia and neutropenia accounted for 32.5% and 34.1%, respectively. However, the rate of grade 3 and grade 4 leukopenia and neutropenia was only 1.4%. Most neutropenia events occurred after 4 to 6 cycles. The rate of anemia was 33.2%; in which most of them were in grade I, accounting for 30.4%. Only 2 out of 56 patients (3,6%) had grade 3 anemia. However, the decrease in hemoglobin was not only due to chemotherapy side effects, but also could be attributed to malnutrition caused by compression of the esophagus and anorexia[15].This also raised the important issue of nutritional care for late stage cancer patients. Rate of thrombocytopenia in all treatment cycles was only 1.9% and all were in grade 1. Another study also had similar result with the very low rate of thrombocytopenia [9].

The side effects on the gastrointestinal tract are usually mild, mainly in grade 1. In this study, nausea/vomiting was the most common gastrointestinal side effect. When using a dose more than 95% of the standard dose, the incidence of this side effect was two times higher than when using lower dose (23.1% vs 11.8%). However, all patients recovered well with the use of supportive drugs and did not require treatment delay.

Side effects on the liver and kidney are uncommon. Rate of AST or ALT elevation was 20.8%, mainly in grade 1. There was no case of grade 3 or 4 liver enzymes elevation. Renal toxicity was much less common with the rate of grade 1 creatinine elevation was only 1.2% of the total 428 treatment cycles, and there was no case of grade 2, 3 and 4.

Thus, the overall side effects of this regimen were infrequently encountered and mild. Most of them can be overcome or prevented without dose reduction or delaying treatment. Given its safety and efficacy, vinorelbine monotherapy was one of the suitable options for patients with recurrent NSCLC after progressing on platinum-based chemotherapy or having contraindication to platinum agents, especially in elderly patients with poor performace status.

## V. CONCLUSION

Vinorelbine is an effective option in recurrent lung cancer patients progressing after platinum-based chemotherapy, with a disease control rate of 76.8% and median PFS of 5.3 months. The regimen was well tolerated, in which no patient had to discontinue treatment due to drug toxicity. The most common side effect was leukopenia and neutropenia, mainly in grade 1. All side effects on the hematopoietic system were recoverable and did not delay the treatment course. Other nonhematologic adverse events were mild and reversible after using supportive drugs.

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