Analysis of Chemotherapeutic Protocols Efficiency in Therapy of Advanced Non Small Cell Lung Cancer

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ORIGINAL PAPER

SUMMARY
Aim: To confirm the efficiency and toxicity of two chemotherapeutic protocols - Cisplatin Gemcitabin (CDDP, Gemcitabin) and Cisplatin, Vinorelbin (CDDP, Vinorelbin) in advanced non-small cell lung cancer (NSCLC). Patients and methods: Retrospectively were analyzed and treated a total of 60 patients (two groups with 30 patients) for advanced or metastatic NSCLC during the period from January 2005 to January 2007. The patients were treated with chemotherapeutic protocols CDDP, Vinorelbin and CDDP, Gemcitabin for four weeks. The chemotherapy was administered intravenously. Results: Although registered response rates were a bit lower than in previously published trials, they were not significantly different in two arms (26% vs. 15%) (p=0.485). Statistically different were therapeutic responses in SD (CDDP, Vinorelbin 44% vs. CDDP, Gemcitabin 93.3%) (p < 0.001) and OS (CDDP, Vinorelbin 10.83 % vs. CDDP, Gemcitabin 21.00%) (p = 0.05). Cisplatin, Vinorelbin regimen has shown a higher hematologic (9% vs. 7%), and total toxicities (p=0.0029). Conclusion: In this investigation of two groups of patients, Cisplatin, Gemcitabin regimen has shown better efficiency and toxicity profile. Preferred regimen could be Cisplatin, Gemcitabin.

Keywords: chemotherapy, Cisplatin, Gemcitabin, Vinorelbin, small cell lung cancer

1. INTRODUCTION
Lung cancer occurs in the bronchial wall and lung cells and for its development is needed many years; given that the transformation of normal cells into neoplastic need more genetic changes. During 2003 lung cancer was second disease in both sexes, but in the same year was also the leading cause of death from malignant disease in men and women. So, it was in front of mortality from breast cancer in women. Since 1995, when the meta-analysis is published, it is known that the extension of survival in these patients can be improved by applying chemotherapy, so that chemotherapy is only one modality of treatment for patients suffering from lung cancer with metastasis to distant organs.

In late eighties, lung cancer is treated by monotherapy. With the discovery of the second-generation drugs Cisplatin and Carboplatine achieved are revolutionary results for that period (1,2,3,4,5,6,7). But the biggest discovery is of the third generation of drugs Taxani, Irinotecan, Pemetrexed, Vinorelbin and Gemcitabin that show high activity applied in patients with non small cell lung cancer (8,9,10,11,12,13).

2. AIM
The aim of this study was to compare two chemotherapy protocols and to determine which of them has a higher efficacy and less toxicity.

3. MATERIALS AND METHODS
Research is carried out retrospectively on the Oncology Department of the Hospital Center „Bezanijska Kosa”, Belgrade, Serbia and the Department of Pulmonary Diseases Slavinovici, Tuzla, Bosnia and Herzegovina in the period January 2005–January 2007 on 60 patients (divided into two groups by 30) due to advanced or metastatic non small cell lung cancer.

Patients were treated with two different chemotherapy protocols Cisplatin, Vinorelbin-(cisplatin 100 mg/m2 D1, Vinorelbin 30 mg/m2 D1, D8 during four weeks)-Belgrade and Cisplatin, Gemcitabin (cisplatin 100 mg/m2 D1, Gemcitabin and 1000 mg/m2 D1, D8, D15 four weeks)-Tuzla. Chemotherapy was ordained intravenously. The study included patients with histology confirmation of the on small cell lung cancer, whose disease was presented in a stage of locally advanced or metastatic non small cell lung cancer.

In all patients analyzed are the rate of response, total survival and overall toxicity.

Toxicity was evaluated as hematological (CBC, DKS-anemia, thrombocytopenia, leucopenia gr. I-gr. IV) as non hematological (neurotoxicity, nephrotoxicity, and alopecia hepatotoxicity).

Therapeutic response was evaluated by repeating the initial diagnostic procedure after every 2nd Cycle (X-ray of the lungs, CT of the thorax, abdomen US).

Survival was calculated from the date of the first cycle chemotherapy, date of lethal outcome of any cause, and
if this information is not known, the last date of control examination.

Of statistical methods were used X2 test, Kaplan-Meier curve and Log rank test.

4. RESULTS

Analyzed are a total of 60 patients divided into two groups of 30 patients

Group A: 30 patients who were treated by CDDP protocol, Vinorelbin 30 patients-Belgrade

Group B: 30 patients who were treated by CDDP protocol, Gemcitabin Tuzla

In the group of patients who received CDDP (Cisplatin) Vinorelbin, 24 patients (80%) were male and 6 (20%) females, while in the group who received CDDP, Gemcitabin 25 patients (83.3%) were male, and 5 patients (16.7%) females, without statistically significant differences.

The median age of respondents of CDDP group, Vinorelbin was 59 (45 to 72 years) and CDDP groups of respondents, Gemcitabin 54.50 (39 to 75 years), also without statistically significant differences.

The general status of patients assessed by Karnofsky scale is significantly different in the two groups of subjects: CDDP, Vinorelbin—100%, 94% of patients, 90%, 3% of patients and 80% 3% of patients, CDDP, Gemcitabin—100%, 33.3% patients, 90%, 40% of patients and 80% of 26.7%. The difference is statistically significant in favor of patients on protocol CDDP, Vinorelbin.

5. DISCUSSION AND CONCLUSION

The group of second-generation drugs is consisted of Cisplatin and Carboplatin which in the treatment of non small cell lung cancer achieve revolutionary results for that period (1,6,8,10,11,12,13,14,15,16). Publication of a meta analysis in which is analyzed use of Cisplatin chemotherapy compared to best supportive therapy, which showed that Cisplatin-based chemotherapy reduces the risk of death by 27%, giving an absolute benefit of 1-year survival of 10%, this type of chemotherapy become the gold standard in treating inoperable non small cell lung cancer (15).

In studies with new drugs in addition to efficiency, compared is the quality of life of patients and all studies have shown that chemotherapy improves quality of life of people with non small cell lung cancer (11). In the last decade has proven that several new drugs, of so called third generation showed high activity applied in patients with non small cell lung cancer (12,14,17,18,19). The third generation drugs include Paclitaxel, Docetaxel, Irinotecan, Topotecan, Vinorelbin and Gemcitabin. Two meta analyses concluded that the standard in the treatment of non small cell lung cancer should be doublets (16,17,19).

![Figure 1. The difference in the overall toxicity of two chemotherapy protocols](image-url)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CDDP/Vinorelbin (N=30)</th>
<th>CDDP/Gemcitabin (N=30)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender Male</td>
<td>24</td>
<td>80</td>
<td>25</td>
</tr>
<tr>
<td>Gender Female</td>
<td>6</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Age mean range</td>
<td>59</td>
<td>45–72</td>
<td>54,50</td>
</tr>
<tr>
<td>Performance status</td>
<td></td>
<td></td>
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<tr>
<td>100%</td>
<td>28</td>
<td>94</td>
<td>10</td>
</tr>
<tr>
<td>90%</td>
<td>1</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>80%</td>
<td>1</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Pathohistology diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>14</td>
<td>47</td>
<td>19</td>
</tr>
<tr>
<td>Planocellular</td>
<td>16</td>
<td>53</td>
<td>9</td>
</tr>
<tr>
<td>Gigantocellular</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
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<tr>
<td>Locally advanced</td>
<td>13</td>
<td>43</td>
<td>5</td>
</tr>
<tr>
<td>Metastatic</td>
<td>17</td>
<td>57</td>
<td>25</td>
</tr>
<tr>
<td>No. of applied cycles mean range</td>
<td>4.23</td>
<td>2–8</td>
<td>3.63</td>
</tr>
</tbody>
</table>

**Table 1. Characteristics of the examined patients**

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>CDDP/Vinorelbin</th>
<th>CDDP/Gemcitabin</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Therapeutic response</td>
<td></td>
<td></td>
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<tr>
<td>CR – complete response</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>PR – partial response</td>
<td>4</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>SD – stable disease</td>
<td>13</td>
<td>44</td>
<td>28</td>
</tr>
<tr>
<td>PD – progression of disease</td>
<td>12</td>
<td>40</td>
<td>1</td>
</tr>
<tr>
<td>PFS – progression free survival Median Range</td>
<td>5.63</td>
<td>2 - 12</td>
<td>6.00</td>
</tr>
<tr>
<td>OS – Overall survival Median Range</td>
<td>10.83</td>
<td>6 - 15</td>
<td>21.00</td>
</tr>
</tbody>
</table>

**Table 2. The efficiency of two chemotherapy protocol**
In this study registered are the response rates somewhat lower than the rate of response in previously published studies, but somewhat lower values are registered in both therapeutic groups. Combination of CDDP response rates, Vinorelbine in previously published studies have ranged around 26%, while in this study registered response rate is of 15%. The reason, of course, lies in the stage of disease, pathohistological type of tumor and metastasis distribution (2,6,8,11).

Statistically significant difference in this study is registered in the therapeutic response in the overall survival and the overall toxicity in general.

Stable disease had 93.3% of patients in the regime of CDDP, Gemcitabin, and the regime of CDDP, Vinorelbine 44% of patients.

Advantage in overall survival has chemotherapy protocol CDDP, Gemcitabin 21.00%, in contrast to CDDP protocol, Vinorelbine whose overall survival rate is 10.83%.

Given that the treatment of locally advanced or metastatic non small cell lung cancer is only a palliative, besides efficiency must be taken into account the toxicity of chemotherapy, and the quality of life of patients suffering from non small cell lung cancer.

REFERENCES