Analysis of Chemotherapy and Molecular Therapy Efficiency in Advanced or Metastatic Non-Small Cell Lung Cancer

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Aim: To compare a benefit of chemotherapeutic protocols Docetaxel with Tarceva molecular therapy in advanced or metastatic non-small cell lung cancer (NSCLC). Primary endpoint- OS (Overall survival), Toxicity. Secondary endpoint- Quality of life. Patients and methods: In this retrospective and -prospective study a total of 63 patients (two groups- 30+33 patients) were analysed and treated for advanced or metastatic NSCLC during the period 2008-2010. One group was treated with molecular therapy Tarceva oral, and the other group was treated with chemotherapy Docetaxel monotherapy every three weeks. The chemotherapy was administered intravenously. Monitoring parameters included overall survival and toxicity. Results: Statistical difference was registered in histology type, total toxicity and total survival. Adenocarcinom occured as a more often pathohistologic type in both groups of patients (Tarceva 57,6% vs Docetaxel 83,3%). The chemotherapeutic protocol, Docetaxel monotherapy, demonstrated higher total toxicity than Tarceva molecular therapy (hematological toxicity grade II 69.0 % Docetaxel vs 12.5 % Tarceva). Tarceva molecular therapy demonstrated longer overall survival (OS) than Docetaxel (Tarceva 26,4 months vs Docetaxel 15,5 months). Conclusion: In this investigation of two groups of patients the molecular therapy Tarceva was showed better efficiency and toxicity profile. Preferred regimen could be molecular therapy Tarceva. Key words: non-small lung cancer, chemotherapy, molecular therapy.

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1. INTRODUCTION
Lung cancer occurs in the bronchial wall and lung cells and it develops over a period of many years. Numerous studies and meta-analyses have shown that chemotherapy is only one modality of treatment of these patients (1). Generally, this type of treatment is not curative and must take into account the quality of life of these patients (2). According to the data of the Surveillance, Epidemiology and End Results SEER Program NCI, USA, 2003. lung cancer was on the second place of morbidity, and also on the first place of mortality among malignant diseases in both genders (3). Every year 1,5 milion new patients with lung cancer are registered worldwide (4). The major risk factor is smoking which is responsible for ninety percent of lung cancer cases. A person smoking pack of cigarettes has twenty times higher risk for lung cancer (5).

Cispaltin and Carboplatin are two powerfull medicines in the NSCLC therapy (6, 7). However, the biggest discovery was of the first generation drugs: Paclitaxel, Docetaxel, Pemetrexed, Iritotecan, Topotecan, Vinorelbine and Gemcitabin which showed the biggest efficiency in the treatment of such patients (8, 9, 10, 11, 12, 13, 14).

2. AIM
The aim of this study was to compare two different protocols and deter-
mine which of them has higher efficacy and less toxicity.

3. PATIENTS AND METHODS
In this retrospective/prospective study we included a total of 63 patients with advanced or metastatic NSCLC/III B or IV/ divided in two groups in the period 2008-2010. One group of 33 patients was analysed and treated with Tarceva molecular monotherapy. In the same period, the other group of 30 patients were treated with chemotherapy protocol Docetaxel monotherapy. Therefore, patients with locally advanced or metastatic NSCLC were treated with two different protocols in two different medical centers.

The treatment plan was that the first group of patients received Tarceva 150 mg one tablet daily, one hour before or two hours after meal until progression or until serious toxicity. The second group received Docetaxel 75 mg/m² chemotherapy intravenously every three weeks (with pre and post medication of Dexamethasone).

We analyzed total toxicity and total survival in all patients.

Toxicity was evaluated as hematological (CBC, DKS-anemia, trombocytopenia, leucopenia grade 1-IV), as non-hematological (neurotoxicity, skin changes-alopetia grade 1-IV, nail changes, rush, bula, eruptions, gastrointestinal perforations-vomiting, diarrhoea grade I-IV, pain in the eye, keratoconjunctivitis sicca).

Therapeutic response was evaluated by repeating the initial diagnostic procedures after every 2nd Cycle (X-ray, CT-Computed Tomography of the thorax, ultrasound of abdomen).

Survival was calculated from the date of the beginning of disease until the date of lethal outcome of any cause or until the date of the last control examination. Statistical methods that were used included X² test and Log rank test.

4. RESULTS
A total of 63 patients divided into two groups were analysed. The first group: 33 patients treated with Tarceva molecular monotherapy.

The second group: 30 patients treated with chemotherapy, Docetaxel monotherapy.

In the first group of patients who received Tarceva 20 patients (60.6%) were male, and 13 patients (39.4%) were female.

In the second group of patients who received Docetaxel 25 patients (83.3%) were male and 5 patients (16.7%) were female, without statistically significant differences.

Also, statistically significant differences were registered in hematological toxicity. Hematological toxicity grade I was noted in 7 patients (87.5%) on the Tarceva and in the second group on Docetaxel in 1 patient (3.4%). Hematological toxicity grade II occurred in 1 patient (12.5%) on the Tarceva and in the second group on Docetaxel 20 patients (69.0%).

None of the patients on the Tarceva had hematological toxicity grade III and in the second group on Docetaxel it was noted in 8 patients (27.6%) (Figure 3).

Figure 3. Pathohistological types of tumours

Figure 4. The difference in hematological toxicity among two protocols

Otherwise, Tarceva demonstrated less toxicity than Docetaxel. Statistically significant differences were registered in non-hematological toxicity. 15 patients on the Tarceva had one non-hematological toxicity and 29 patients on Docetaxel.

Non-hematological toxicity grade I occurred in 13 patients on the Tarceva and in the second group on Docetaxel none of the patients had it. Non-hematological toxicity grade II was noted in 2 patients on the Tarceva and in the second group on Docetaxel no patients had
it. Non-hematological toxicity grade III occurred in 3 patients on the Tarceva and none from the second group on Docetaxel.

None of the patients on the Tarceva had non-hematological toxicity grade IV and in the second group on the Docetaxel it was noted in 1 patient (Figure 5).

5. DISCUSSION AND CONCLUSION

The hemotherapeutics in the treatment of NSCLC are divided into three generations.

The second generation consists of Cisplatin and Carboplatin which achieve excellent results in the treatment of NSCLC for that period (6, 7, 8, 9, 10, 11, 12, 13, 14, 15).

The third generation consists of Paclitaxel, Docetaxel, Irinotecan, Topotecan, Vinorelbine and Gemcitabine (8, 9, 10, 11, 12, 13, 14). The optimal number of hematological agents was analysed in the several clinical studies and two meta-analyses. The conclusion was that the doublets are the gold standard in the treatment patients of NSCLC (15). In this study statistically significant differences were registered in pathohistological type of tumours, total toxicity and total survival. Adenocarcinoma occurred more often as a pathohistological type in both groups of patients. In the first group treated with Tarceva adenocarcinoma was registered in 57.6% of patients and in the second group on Docetaxel in 83.3% patients. Tarceva molecular monotherapy has shown less toxicity than Docetaxel.

Hematological toxicity grade II was noted in 12.5% of patients on Tarceva and 69.0% on Docetaxel.

More non-hematological toxicity was registered in patients on Tarceva than on Docetaxel. Non-hematological toxicity grade I occurred in 39.4% of patients on Tarceva but that toxicity was described and expected and does not lead to significant exacerbation of the general status of patients like in those receiving Docetaxel.

In addition this study registered statistically significant differences in total survival between Tarceva and Docetaxel. Again, Tarceva has shown superiority over Docetaxel. The total survival in the first group on Tarceva was 26.4 months and in the second group on Docetaxel it was 15.5 months.

The quality of life is a very important fact. The quality of life is a very important factor for patients with NSCLC. Therefore, in addition to efficiency we took into account the toxicity of the therapy. In respect to these two criteria a preferred protocol could be the Tarceva molecular therapy.

REFERENCES


5. Staudt R, Camp C, Provencia M, Isla D. Rosell R, Vadell M. et al. Non-hematological toxicity grade I occurred in 39.4% of patients on Tarceva but that toxicity was described and expected and does not lead to significant exacerbation of the general status of patients like in those receiving Docetaxel.

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