

## ROLE OF CHEMOTHERAPY IN COMBINED TREATMENT OF PATIENT WITH IIB-III A STAGE OF NON-SMALL CELLS LUNG CANCER

Summary. Results of neoadjuvant polihimioetrapii in patients with small cell lung cancer is published in this article. Based on the results of the observations concluded that in patients with stage IIB-III non-small cell lung cancer neoadjuvant chemotherapy is effective. The sum of complete and partial regression of the tumor was 70.4%. The toxicity of the treatment was acceptable, without severe complications. The median life expectancy for patients in the intervention group increased to 15.6 months compared to 11.5 months for the control group ( $p < 0.05$ ). It is concluded that the use of neoadjuvant chemotherapy is an effective way to improve the immediate and long-term results of treatment of patients with small cell lung cancer stage IIB-III.

**Key Words:** non small lung cancer, neoadjuvant chemotherapy, surgery.

Lung cancer remains the most common form of cancer in the world. In Ukraine the crude sickness rate is 35.8 per 100 thousand of population. 63.3% of newly diseased have not lived for 1 year. Non-small cells lung cancer (NSCLC) is detected in approximately 80% of cases. Unfortunately, at first seeking medical advice more than a third of patients with NSCLC are diagnosed with III stage disease. Today, the “standard” for the treatment of III stage NSCLC is considered the integrated approaches that include radical surgery, chemotherapy, and external beam radiotherapy. However, the survivability of patients with advanced-stage NSCLC remains low. After radical surgery only, the 5-year survivability rate does not exceed 10-15%. A large number of clinical trials of the last decades were aimed at application of methods improving long term findings, including the research of the effects of neo-adjuvant and adjuvant polychemotherapy, and combinations thereof.

The experience of recent years of the use of neo-adjuvant polychemotherapy (NPCT) in NSCLC has showed no increase in the frequency of postoperative complications and mortality compared with only surgical treatment, as confirmed

by numerous international randomised multicentre studies. So, it has emerged a moral right to develop and apply various schemes of NPCT.

The objective of our research is to research the effect of neo-adjuvant polychemotherapy on not only short-term, but also on the immediate and long-term findings of treatment of IIB-III stages of non-small cells lung cancer.

In the last 5 years we have observed 290 patients with stage IIB-III NSCLC, who were treated at the R&D works over the past 5 years. For a comparative analysis all of them are divided into two groups. The first - index group included 123 patients who received first NPCT, and after the evaluation of its findings underwent the surgical treatment. The second - the control group consisted of 167 patients who underwent only surgery. The characteristics of patient groups are shown in Table 1.

Neo-adjuvant polychemotherapy for our patients consisted of 2-3 cycles of administering cytostatic agents. According to the treatment standards the main drug was platinum-based drugs (Cisplatin or Carboplatin). Cisplatin in a dose of 80 mg/m<sup>2</sup> in combination with 25 mg/m<sup>2</sup> of Vinorelbine, 1250 mg/m<sup>2</sup> of Gemcitabine, 175 mg/m<sup>2</sup> of Paclitaxel and 120 mg/m<sup>2</sup> of Etoposide. The surgical intervention in the research group was performed no later than three weeks after the last cycle of NPCT.

Surgical interventions in the radical volume (lobectomy, bilobectomy, pneumonectomy) were combined with elimination of lymph node basins. The volume of surgical interventions in the groups under research is presented in Table 2.

Statistically significant differences ( $p > 0.05$ ) between the groups in terms of surgical procedures have not been observed.

### **Findings and their discussion**

In the index group, all patients were evaluated for the effect of neo-adjuvant treatment. The dynamics of change in tumour size and lymph nodes was recorded after NPCT on the basis of performed CT. The effectiveness of the treatment was determined by RESIST criteria, and the toxicity of polychemotherapy was evaluated upon the CTC-NCIG scale.

The objective clinical effect (the sum of complete and partial tumour regression) was observed in 70.24% of patients, and the process stabilisation - in 29.76%. Complete regression of the tumour as a result of NPCT was observed in

7.24% of patients (the tumour could not be detected not only during CT examination, but also perioperatively).

With the effective NPCT the tumour and regional metastases have significantly retracted, allowing a radical intervention even in cases where the patients before the treatment were considered as conditionally operable.

Conducting NPCT improved the operability of patients. Thus, the index group out of 123 patients operated all interventions were radical. Prior to NPCT 36 of them were considered conditionally operable. Improving resectability is due to the effect of the NPCT held, which is in agreement with literature data. According to our data, as well as literature data, conducting special preoperative treatment did not increase the number of postoperative complications and worsen the operative mortality. Thus, the frequency of bronchial fistulas in the index group was 6.2%, while in the control group - 6.4%. Postoperative mortality in the index group was 2.06%, and in the control group - 2.4%.

It has also been studied the afterhistory of treating patients with NSCLC of the index and control groups. It has been evaluated the survival index of patients: average-expectancy life meridian and three-year survival rate. The average-expectancy life meridian in the case of NCT increased to 15.6 months compared to 11.5 months for the control group ( $p < 0.05$ ). A similar improvement was also observed in terms of one-, two- and three-year survival rate, so in the index group it was 61.5%, 27.5% and 21.4%, respectively, and in the control group - 53.4%, 24% and 16, 3% respectively. However, there was no statistically significant difference between.

According to the findings, the histotype of tumour had no effect on survival rate of radically operated patients both in the index and control groups.

### *Conclusions*

On the basis of observations using NCT for patients with IIB-III stage NSCLC is the basis to conclude that the NCT ofon the basis of platinum-based drugs with new generation chemotherapeutic agents produces a quite effective influence on the primary tumour and regional metastases - the sum of complete and partial regression of the tumour was recorded in 70 4% of patients. Toxicity of chemotherapeutic agents used was quite acceptable, with no serious complications.

According to our data, NPCT on the basis of platinum-based drugs with gemcitabine or vinorelbine or docetaxel did not affect the rates of postoperative

complications and postoperative mortality, which is consistent with data from other authors.

Preliminary findings of our research indicate that patients who received the NPCT drugs of new generation had increased operability and a tendency to increase survivability.

Thus, on the basis of the research and analysis of literature data, we can conclude that the use of NPCT on the basis of platinum-based drugs and new generation drugs is an effective way to improve the short-term results and afterhistory of treating patients with stage IIB-III NSCLC.

Table 1. The characteristics of patient groups are shown.

	Index group (N-123)	Control group (N-167)
Men	94(76,4%)	121(72,5%)
Women	29(23,6%)	46(27,5%)
Middle age (r)	57	59
Stage 2	35(28,47%)	42(25,2%)
Stage 3A	82(66,66%)	122 (73%)
Stage 3B	6(4,87%)	3(1,8%)
Adenocarcinoma	43(34,96%)	38(22,7%)
squamous cell carcinoma	69(56,1%)	122(73,1%)
Dimorph tumor	11 (8,94%)	7 (4,2%)

Table 2. The volume of surgical interventions in the groups under research is presented.

Объём операции	Index group (N-123)	Control group (N-167)
Lobectomy	53 (43,1%)	51 (30,5%)
Bilobectomy	6 (4,9%)	20 (11,9%)
Pneumonectomy	64 (52,0%)	96 (57,6%)