

## ORIGINAL ARTICLE

# CORRELATION OF RELAPSE-FREE SURVIVAL WITH NEOADJUVANT TREATMENT IN PATIENTS WITH STAGE IIIA NON-SMALL CELL LUNG CANCER

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## ABSTRACT

**The aim:** The aim of this study was to investigate disease-free and overall survival in patients with stage IIIA NSCLC after neoadjuvant chemotherapy, neoadjuvant chemoradiotherapy, and neoadjuvant chemotherapy.

**Materials and methods:** For the study, 3 groups of 65 people were taken. All patients underwent radical surgery in the form of lobectomy, bilobectomy or pneumonectomy. All groups received 3 or 4 courses of neoadjuvant chemotherapy according to the scheme Docitaxel (Paclitaxel) and Cisplatin (Carboplatin), while groups II and III also received, respectively, neoadjuvant and adjuvant radiation therapy in the amount of 30 Gy to the chest and mediastinum. Survival was assessed using the Kaplan and Mayer scale.

**Results:** 1. At a survival period of 6 months, the results of relapse-free survival in the NCRT and NCT groups do not differ. 2. From 12 months to 5 years, the highest recurrence-free survival rates are observed in the NHL group. 3. The overall five-year survival rate in the main group was  $28.1 \pm 5.9\%$ , in the NCT group -  $10.4 \pm 3.8\%$  and -  $5.8 \pm 2.0\%$  in the NCT + RT group.

**Conclusions:** The best recurrence-free survival results are observed in the NHL group. Also, the largest number of cases of molar morphological response, correlated with the highest survival rates, also occurs in the NHL group.

**KEY WORDS:** Non-small cell lung cancer, neoadjuvant therapy, chemoradiotherapy, chemotherapy, overall survival

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## INTRODUCTION

Treatment of stage IIIA non-small cell lung cancer remains a difficult problem today. There was no unified strategy on this issue. In order to identify the optimal method for the treatment of this pathology, it is necessary to analyze the overall and relapse-free survival with existing treatment methods:

Lung cancer is a common type of disease in the world and the main cause of death in men.

Etiological causes of the disease:

1. Smoking - 85% of non-small cell lung cancer is associated with smoking;
2. Radon exposure;
3. Asbestos;
4. Dust pollution;
5. Ionizing radiation on the chest area in the anamnesis;
6. Inhalation of air contaminated with metals and polycyclic hydrocarbons;
7. Pulmonary fibrosis;
8. Human immunodeficiency virus;
9. Heredity [1,2].

Small cell lung cancer is treated with chemotherapy, targeted therapy and immunotherapy, and non-small cell lung cancer is treated with neoadjuvant chemotherapy

or chemoradiotherapy and radical surgery, if necessary, adjuvant chemo or radiation therapy is performed [1].

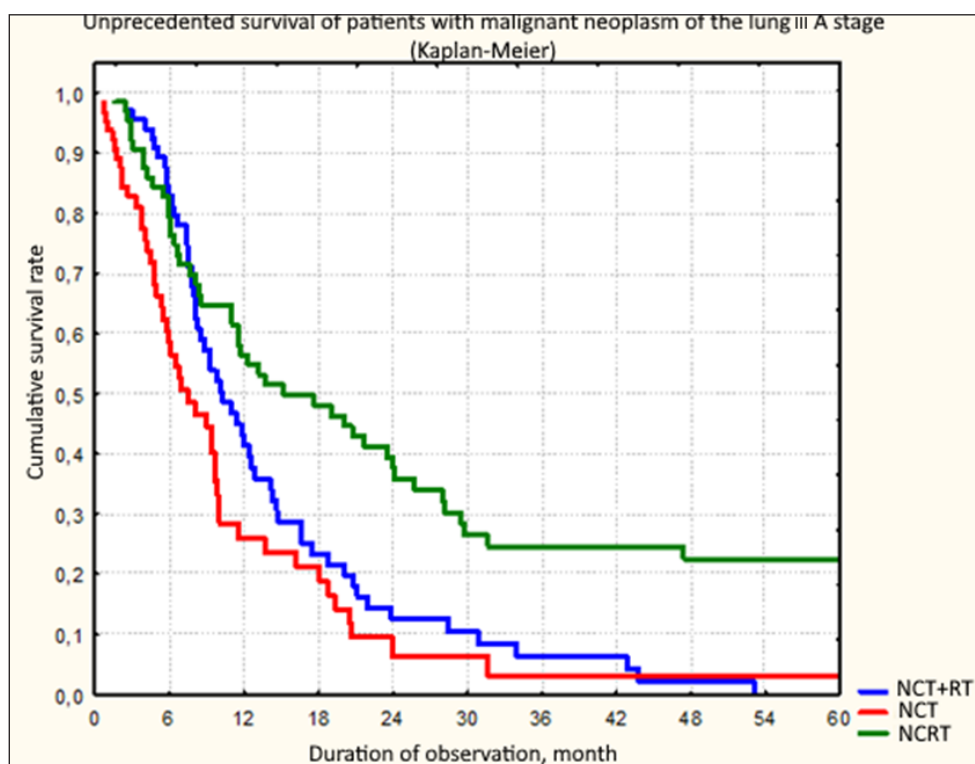
Survival in stage IIIA of non-small cell lung cancer remains low even after a full course of treatment - 58% of patients do not live a year from the moment of diagnosis [1]. A clear strategy for the treatment of stage IIIA non-small cell lung cancer in some cases is dual or absent altogether. For example, the NCCN clinical protocol of 2020 shows the possibility of neoadjuvant chemoradiotherapy or neoadjuvant chemotherapy and adjuvant radiation therapy without specifying the number of courses and radiation regimen, and in the clinical protocols of the CIS countries they are mandatory and at least 3 courses of neoadjuvant chemotherapy are carried out. Radiation therapy is not considered mandatory [2,3].

The literature data found on pub med indicates that over the past 20 years, a large number of studies have been conducted, both case-control and retrospective studies, as well as randomized clinical trials and meta-analyses [4-6]. The research results are contradictory. Some indicate an increase in survival with the use of neoadjuvant chemoradiotherapy, others indicate that there is no difference with both methods. There is evidence that the use of chemoradiotherapy increases the likelihood of a complete morphological response (a

**Table I.** Cumulative relapse-free survival with different methods of treatment of patients with stage III A of NSCLC

Survival time	Treatment methods		
	NHL	NHT	NHT + LT
6 months	79.52 ± 5.06	59. ± 6.4	82.9 ± 4.7
12 months	56.6 ± 6.3	27.5 ± 6.3	42.3 ± 6.4
36 months	24.6 ± 5.7	0	6.5 ± 3.5
5 years	19.5 ± 5.4	0	0

Cumulative relapse-free survival with different methods of treatment of patients with stage III A of NSCLC



**Fig. 1.** Cumulative unprecedented patient survival with malignant neoplasm of the lung III A stage

phenomenon when, after neoadjuvant treatment, areas of fibrosis are observed on the site of cytologically or histologically confirmed malignant cells), and a complete morphological response, in turn, is associated with an increase in survival. Perhaps such contradictory results are based on the lack of standardization of the number of courses of chemo and radiation therapy, the dosage of radiation therapy, types of linear accelerators and drugs for chemotherapy [2-8].

It should be noted that there is no convincing data in the literature on relapse-free survival in stage IIIA non-small cell lung cancer using different methods of neoadjuvant therapy [8-12].

It becomes obvious that it is necessary and promising to study the effectiveness of methods of neoadjuvant chemotherapy and chemoradiotherapy for stage IIIA non-small cell lung cancer under the conditions of standardized treatment and relapse-free survival for each of the methods.

**THE AIM**

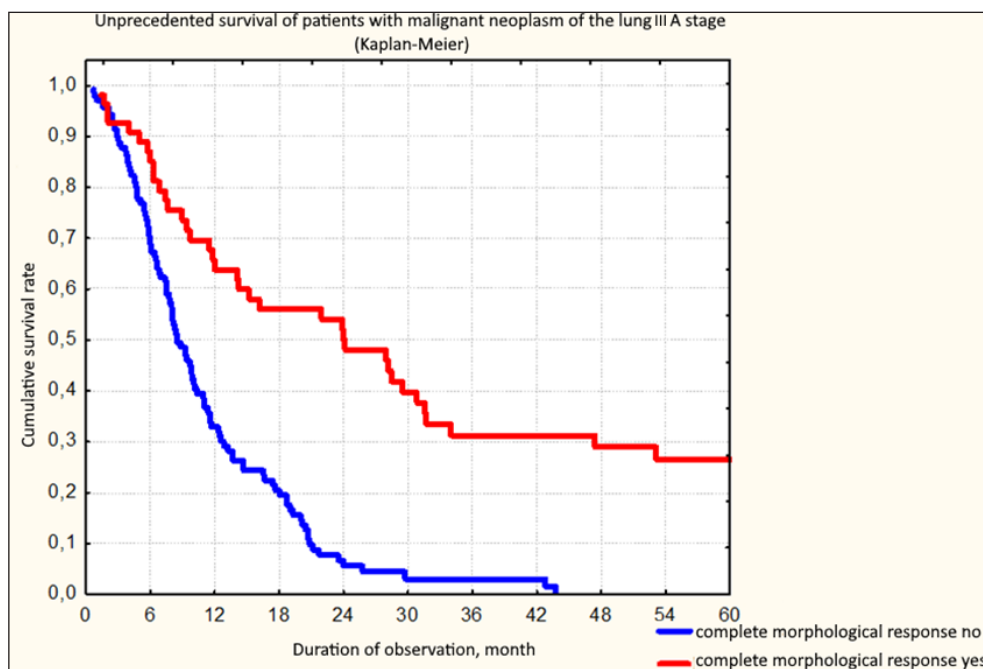
The aim was to determine the relapse-free survival in patients with stage IIIA NSCLC after various types of neoadjuvant and adjuvant treatment.

**MATERIALS AND METHODS**

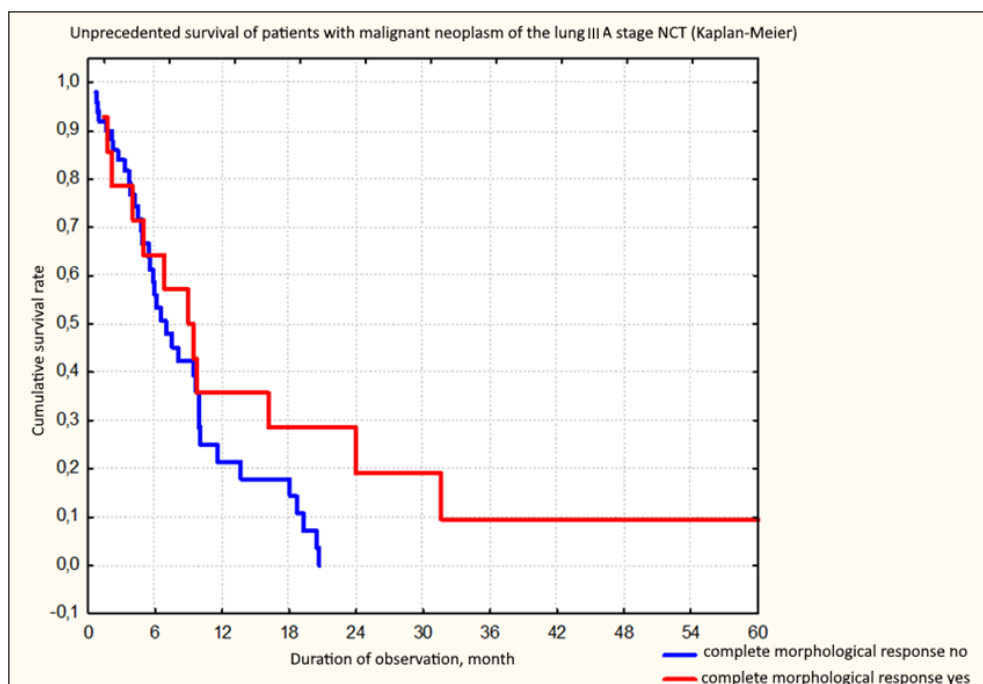
The work was carried out on the basis of the Department of Chest and mediastinal tumors of the National Cancer Institute, Ukraine. For the study, 3 groups of patients with stage IIIA NSCLC were taken, each of which consisted of 65 people. All patients underwent radical surgery in the volume of lobectomy, bilobectomy or pneumonectomy. The first group of patients received neoadjuvant chemoradiotherapy, the second group received neoadjuvant chemotherapy, the third group received neoadjuvant chemotherapy and adjuvant radiation therapy. Neoadjuvant radiation therapy was carried out in the amount of 30 SOD GY with a single dose of 2 GY, chemotherapy was 3-4 courses with Carboplatin or Cisplatin and Docetaxel or Paclitaxel.

The volume of examinations of patients in all 3 groups was standard:

- A general blood test;
- Biochemical blood analysis;
- Coagulogram;
- Blood type and Rh factor test;
- Gastroscopy;



**Fig. 2.** Cumulative unprecedented survival of patients with malignant neoplasm of the lung III A stage NCT (Kaplan-Meier)



**Fig. 3.** Cumulative unprecedented survival of patients with malignant neoplasm of the lung III A stage NCT+RT (Kaplan-Meier)

CT of the chest, abdominal cavity and pelvis with intravenous contrast before treatment and before surgical treatment. After the treatment, the patients remained on the dispensary register.

Relapse-free survival was studied in all 3 groups. It was evaluated on the Kaplan and Major scale [13-17].

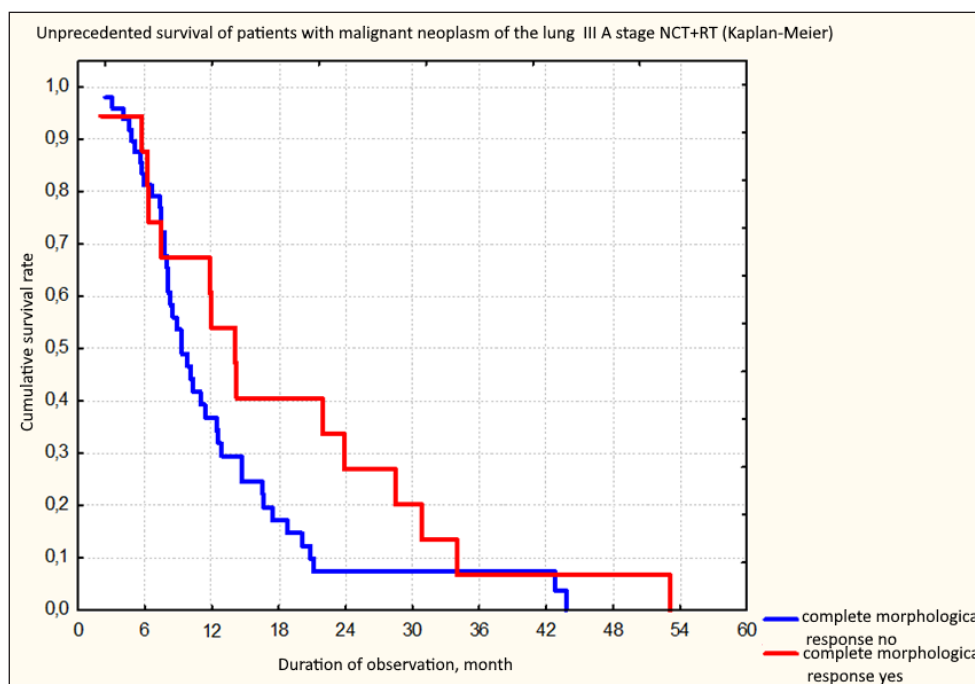
## RESULTS

To analyze the effect of different treatment methods, calculations of cumulative relapse-free survival according to Kaplan and Mayer were used, and look like this:

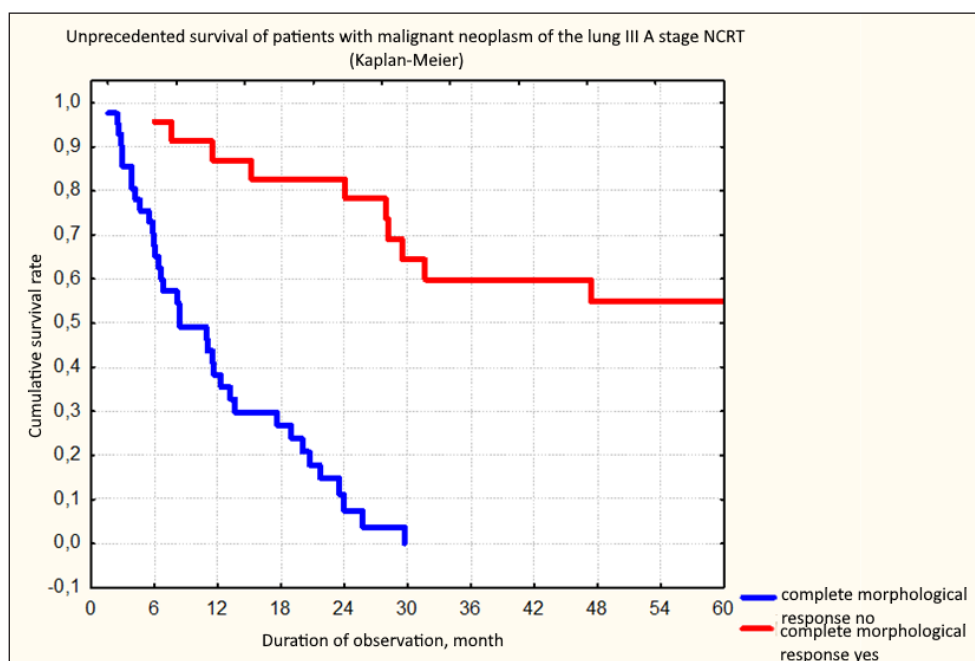
Also installed:

1. At a survival period of 6 months, the results of relapse-free survival in the NCRT and NCT groups do not differ. There are distinct differences in the survival period of 12 months - in the NCRT group, better results are noted than in other groups. The lowest cumulative survival results were observed in the NCT group. At the 36-month survival period, the best results are observed in the NCRT group, the worst results in the NCT+RT group, and there are no cases of relapse-free survival at this time in the NCT group. At a survival period of 5 years, cases of relapse-free survival are noted only in the NCRT group.

2. NCRT shows advantages over other methods of neoadjuvant and adjuvant treatment in the long term.



**Fig. 4.** Cumulative unprecedented survival of patients with malignant neoplasm of the lung III A stage NCRT (Kaplan-Meier)



**Fig. 5.** Cumulative relapse-free survival with different methods of treatment of patients with stage IIIA of NSCLC

3. The overall five-year survival rate in the main group was 28.1±5.9%, in the NCT group - 10.4±3.8% and - 5.8±2.0% in the NCT + RT group.

**DISCUSSION**

To date, no single strategy has been identified for the treatment of stage IIIA NSCLC. NCCN assumes 3 main strategies - NCRT, NCT and NCT +RT, while drugs for chemotherapy are defined, but the dosage of radiation therapy is not indicated [18, 19].

There are many studies in this direction, but they do not give a complete picture of an unambiguous answer. There are case-control studies, non-randomized clinical

trials, randomized clinical trials, meta-analyses that show contradictory results. None of the studies provided a sufficient number of materials with the same drugs for chemotherapy, the number of chemotherapy courses, and radiation therapy dosages. Therefore, some studies show the benefits of NCRT, some studies do not show the difference between NCRT and NCT, some studies show better results with NCT. There are no relevant data for NCT + RT, there are no data on the duration of relapse-free survival in the treatment of stage IIIA NSCLC [18-22].

Our study showed an advantage in relapse-free and overall survival of NCRT compared to other methods. The phenomenon of a complete morphological response was noted. Patients with a complete morphological response

had significantly greater relapse-free and overall survival than the rest of the patients in their group. The predominant number of such patients was registered in the NCRT group.

Also, these studies show a tendency to improve survival in NCRT and further studies are required to prove the benefits of this technique with the identification of the optimal dosage of radiation therapy for patient survival.

## CONCLUSIONS

This study allowed us to draw the following conclusions:

1. The duration of relapse-free survival is directly correlated with the duration of overall survival.
2. At a survival period of up to 6 months, the cumulative relapse-free survival rate is highest in the NCT + RT group, the cumulative relapse-free survival rates for the NCRT and NCT groups do not differ.
3. Since the period of survival of 12 months to the end of the study, the best indicators of relapse-free survival observed in the group NCRT.
4. Patients with the phenomenon of complete morphological response and the phenomenon of a high degree of morphological response had a significantly longer period of relapse-free survival and overall survival than other patients in their group. The largest number of patients with a complete morphological response was found in the NCRT group.

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**Conflict of interest:**

*The Authors declare no conflict of interest.*

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**D** - Writing the article, **E** - Critical review, **F** - Final approval of the article