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ORIGINAL ARTICLE

Significance of Using Capecitabine Combination after Systemic Polychemotherapy in Patients with Triple Negative Breast Cancer

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ABSTRACT
Triple-negative breast cancer (TNBC) is a heterogeneous disease characterized by varied prognosis and sensitivity to anticancer therapy. This variability is due to a range of genetic aberrations leading to the development and progression of the disease. The study included 126 patients with a verified diagnosis of TNBC who received inpatient and outpatient treatment between 2011 and 2017. The patients were divided into three groups: Group 1 consisted of 47 patients who received neoadjuvant polychemotherapy (NPCT), underwent radical surgery, and received radiotherapy (RT) according to the standard method; Group 2 included 43 patients who underwent radical surgery with adjuvant polychemotherapy (APCT) and RT according to the standard method; and Group 3 consisted of 34 patients who received NPCT, followed by radical surgery and RT, along with monochemotherapy with capecitabine. A study of the survival of these patients showed that the 5-year disease-free survival (DFS) rate was 49.5% ± 6.4% for invasive lobular carcinoma, compared with 79.8% ± 3.7% for the nonspecific variant, and 88.2% ± 2.7% for the medullary variant. Similar differences were noted in the analysis of 5-year overall survival (OS), with rates of 73.2% ± 3.9% for the invasive nonspecific type and 62.5% ± 17.6% for the invasive lobular type. The most aggressive histological form was the metaplastic subtype, which had a poor prognosis, with a 3-year DFS of 43.4% ± 3.2% and an OS of 38.2% ± 3.9%, with no patient surviving more than 5 years. In contrast, the medullary and apocrine subtypes showed no signs of disease progression, and the 5-year OS was 97%. Optimal long-term treatment results were achieved with the use of NPCT—a combination of platinum and taxanes—while combinations involving anthracyclines yielded worse results, falling behind standard chemotherapy regimens in terms of long-term outcomes.
***Keywords**: Triple-negative breast cancer, neoadjuvant polychemotherapy, immunohistochemistry*

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INTRODUCTION

Currently, breast cancer is one of the five most common cancers in the world and is the leading cause of death for women under the age of 50. Detection of breast cancer during preventive examinations throughout the country remains low, and the rate of neglect IIIB - IV stage, which is the leading criterion for the quality of diagnosis, on the contrary, is high. The real way to improve the results of treatment of breast tumors is early, and in some cases, preclinical diagnosis. In 25% of cases, breast cancer is diagnosed at reproductive age [1,2,3,5]. More than 1 million new cases of breast cancer are registered annually in the world, the highest incidence is observed in the USA, Canada, France, Israel, Switzerland, Spain, Finland, the Baltic countries, Australia and the Hawaiian Islands. Low incidence rates are observed in the countries of Asia, Africa, South America - in Japan, China, Mexico and Venezuela. According to the American National General Cancer Registry (NCCN), one in 28 -women in the United States dies from

breast cancer, and one in eight is at risk of developing the disease. In 2019 more than 230,000 women in the United States have been diagnosed with breast cancer. In the United States, in 2020, there were 232,332 new cases and 39,620 deaths [13,14,42] .

According to the National Cancer Registry of Ukraine in 2020. 16,504 new cases of breast cancer have been registered; in different regions of the country, the incidence varies from 30 to 61 cases per 100,000 women [9]. About 16,000 new cases of breast cancer are registered annually in Ukraine, and about 8,000 patients die from this disease [11].

In the structure of cancer incidence, breast cancer ranks first among the female population of Russia and the CIS countries. In Russia, at least 54,000 new cases of breast cancer are diagnosed annually [7, 10]. The highest rates were recorded in Moscow - 52.3 and St. Petersburg - 48.1 per 100 thousand women [10]. Its share varies from 18-22% in Russia, Belarus, Kazakhstan and Kyrgyzstan to 25-33% in Uzbekistan, Azerbaijan and Armenia. In Uzbekistan, for several decades, breast cancer has consistently ranked first among women's oncological diseases and is one of the four most common oncopathologies registered among the country's population [12].

The prevalence of malignant tumors of the breast is to some extent related to the demographic characteristics of the population. Breast cancer is the most common cancer among women in Uzbekistan [12]. According to various authors, TN breast cancer occurs in 27-39% of cases of breast cancer [1,19]. Numerous factors influence the development of breast cancer: the state of the reproductive system, genetic, constitutional, alimentary, socio-economic, pathological processes associated with dysfunction of the hypothalamic-pituitary-ovarian system, concomitant diseases. To the latter may include thyroid diseases with hypothyroidism, early obesity with the onset of menstruation before the age of 12, and benign hyperplastic processes of the mammary glands [21,32]. At the same time, it has long been known that an increase in the number of full-term pregnancies contributes to the development of all subtypes of breast cancer, but not TN breast cancer, apparently being an exception to this rule. In addition, some studies have shown that pregnancy increases the chance of developing this subtype of breast tumors [30,33].

The results of studies that have studied this subgroup of diseases indicate a low chance of patients for recovery, as well as a tendency to a negative outcome of the disease in patients with TNBC to a greater extent than in individuals with other tumor subtypes, with worse OS rates and an increased risk of disease recurrence. Among distant metastases, metastasis to the brain and lungs is most likely, less likely to the bones and liver. Observations of patients in this subgroup revealed that the recurrence of the disease develops, as a rule, within the first 3 years after completion of treatment.

At the beginning of the last century, it was enough to know that a patient had a malignant tumor of the mammary gland, then they were prescribed a single treatment. Over time, observations have shown that patients with the same type of cancer show a different prognosis, and the identification by pathologists of the increasing form of various morphological variants of the tumor over the past 50 years has led to a discussion of the classification of breast cancer [18, 26]. On the other hand, pathologists state that breast cancer is a heterogeneous disease with different histological and biological properties due to genetic, epigenetic and transcriptomic changes, with different clinical findings and responses to treatment, and with several subtypes. This phenotypic difference influences the diagnosis, treatment and hence prognosis of breast cancer. All this chaos seems to be based on the absence of specific markers and incomplete understanding of the development of breast epithelial cells [35]. Invasive breast cancer is currently classified as non-specific ductal carcinoma and a specific subtype. The subtypes of breast cancer have certain differences, while the non-specific type includes all types of carcinomas except for certain subtypes. Nonspecific invasive ductal carcinomas account for about 60–75% of all breast cancer cases. Specific types account for 20-25% of all, of which the most common are lobular, tubular, papillary and mucous tumors [36,39].

Histological classification is associated with the histological type of the tumor, as well as the presence of molecular changes, in particular, such as ER and EN with the inclusion of Her-2 amplification [35, 40] .

In the traditional approach, a number of powerful parameters, such as the size of the tumor and the nature of its spread (in particular, the state of the l /nos lesion), determine the stage of the disease, and these are important prognostic factors [21,29,38].

Histopathological evaluation is very effective in the clinical management of patients with breast cancer. However, significant differences are found among patients with the same histological subtype (eg, tubular carcinoma) and the same histological grade - the same stage (eg, node-negative disease) in response to treatment and long-term survival, as well as the benefits of tamoxifen treatment in ER. -positive patients and treatment with trastuzumab in patients with HER-2 amplification all support the belief that breast cancer is a heterogeneous group of diseases, indicating the importance of tumor biological properties in

its treatment . With the beginning of a new era of breast cancer research based on the use of high technologies, it became possible to determine prognostic factors. The development and study of genomic profiling and expression contributed to the development of breast cancer classification systems that included tumor biology rather than morphology [32, 34, 38,39].

Studies have confirmed the idea that breast cancer is a molecularly heterogeneous disease with a different clinical picture, the presence of gene expressions that determine tumor behavior and disease prognosis [20, 25].

TN breast cancer is a heterogeneous disease that is characterized by heterogeneous prognosis and sensitivity to anticancer therapy, which is due to a variety of genetic aberrations leading to the development of the disease and its progression. Triple negative » Breast cancer is a tumor whose cells do not contain estrogen receptors, progesterone and do not have Her2/ neu amplification. According to different authors, tumors of this type account for 15% of all invasive breast cancer, while they are characterized by large sizes and poor prognosis [16; c 60-64]. An interesting pattern of TN in breast cancer and its association with a mutation in the BRCA1 gene was revealed. There is evidence that patients with TN breast cancer are insensitive to chemotherapy, with the exception of platinum drugs [24, 25, 27].

No less important for the correct establishment of the prognosis in patients with TN breast cancer is to take into account the state of receptors not only for estrogens and progesterone, but also for androgens [16,2 4].

TN breast cancer is according to different authors from 11% to 22% all histological variants of cancer of this organ. There is still no consensus on what to consider estrogen-positive tumors - neoplasms in which 10% [21], 5% [17] or even 1% of the nuclei stain positively on IHC. This is due to the lack of rational substantiation of the threshold values for the frequency of cells that give a positive IHC reaction to estrogen receptors (ER). TN breast cancer occurs mainly in young patients and patients in the premenopausal period.

However, unlike other subtypes, TN in the early stages of breast cancer may turn out to be a truly curable disease, in which ACT does not just delay recurrence, but actually completely destroys micro metastases. So, with luminal subtypes, although they are characterized by a more favorable course even at the stage of a widespread disease, after radical treatment and ACT, relapses occur 5-10, sometimes 20 or more years after the completion of treatment. With early TN, the situation is significantly different: in the first 3-5 years after completion of treatment, the risk of progression is incomparably higher than in other subgroups. However, in the future (5-7 years after completion of therapy), the risk of recurrence of the disease in TN BC decreases sharply, and after 7-8 years the survival curve reaches a plateau - relapses of the disease are no longer observed [35,39].

This once again confirms the need for a differentiated approach to the analysis of the results of treatment of early stages of breast cancer, depending on the tumor subtypes. The best results in the treatment of subtypes other than TN BC may be due to the late occurrence of micrometastases due to the low proliferative activity of the tumor and/or long-term survival after their appearance, but not the cure of the disease [10,17]. In the case of TN breast cancer, despite the worst overall results of treatment, a certain cohort of patients can achieve a cure [11].

However, as mentioned above, the most likely explanation is the significant heterogeneity of TN in breast cancer: within the same subgroup, united only by the negative status of three receptors, there are tumors with high sensitivity to chemotherapy and a favorable prognosis and an unfavorable prognosis, tumors that are not sensitive to chemotherapy, but at the same time having a different prognosis [19,23,25]. For example, according to a recently published study, among patients with TN breast cancer, whose tumors did not respond with complete pathomorphological remission to the ongoing NPCT, there is a cohort of patients with a good prognosis due to a favorable genetic subtype of TN in breast cancer. The survival rate of such patients, despite the absence of complete morphological remission of the tumor, was 79.8% versus 48.5% among patients belonging to other subtypes of TN BC.

The second factor causing unsatisfactory results in the treatment of TN in breast cancer is the lack of available therapies for this tumor subtype. Before the advent of targeted therapy, all patients with breast cancer received only chemotherapy, which acts only on rapidly dividing tumor cells of highly aggressive subtypes of breast cancer, while the survival of other patients was due not so much to therapy as to the biological characteristics of the tumor.

Against the background of successes achieved in the treatment of tumors that received additional methods of drug therapy (targeted), a subgroup of patients with TN in breast cancer began to be clearly distinguished, for which the situation has not changed, the only method of their treatment is chemotherapy [7,9].

The preferred chemotherapy regimens for TN breast cancer have not yet been determined, which makes it an extremely difficult clinical task to determine the priority areas of research that are currently being carried out, which also determine the conduct of this study [16, 22]. There is no doubt that from the standpoint of traditional nosological concepts, TNBC is a heterogeneous group, most of which is represented by basaloid cancers, with certain genomic disorders and immunophenotype. When planning the treatment of these patients, it is necessary to use non-standard schemes and regimens for breast cancer. Thus, TN in breast cancer is currently an unsolved scientific and practical problem in the field of oncology, requiring additional research both in terms of finding optimal approaches to the use of already available diagnostic and treatment options, and in searching for new treatment options, as well as fundamental research. in the field of studying the biological characteristics of the disease.
The aim of the study is to improve the diagnosis and treatment of patients with triple-negative breast cancer.

MATERIAL AND METHODS

The work used data from 126 patients with a verified diagnosis of TN in breast cancer, who received inpatient and outpatient treatment in the period from 2011 to 2017. in the conditions of the Tashkent city branch of Oncological center in the departments of oncomammology and chemotherapy. The distribution by stages was as follows: $T_1N_0M_0$ (I st.) - 12 patients (9.5 %) , $T_2N_0M_0$, $T_1N_1M_0$ (II a Art.) - 19 patients (15.1%), $T_2N_1M_0$ (IIb st.) - 29 patients (23%), $T_4N_0M_0$ (III a st.) - 26 patients (20.6%), $T_4N_{1-2}M_0$ (IIIb Art.) - 22 patients (17.5%), $T_4N_3M_0$ (III from Art.) -18 patients (14.3%); and by age: under 35 years old - 22 (17.5%), 35-44 years old - 38 (30.1%), 45-54 years old - 41 (32.5%), over 55 years old - 25 (19.5%). eight%).
A retrospective analysis of case histories and outpatient cards was carried out with an assessment of the results of instrumental and laboratory methods of examination.
When collecting material from primary documentation , anamnestic, clinical, pathomorphological and IHC data were taken into account, with the following included : adjuvant and neoadjuvant chemotherapy, volume of surgical treatment , results of treatment with the study of objective data of clinical and pathomorphological regression, histological and IHC tumor characteristics , date of occurrence of local recurrence, date of death.
The diagnostic stage included carrying out clinical and instrumental research methods with the inclusion of: examination, data from general clinical, biochemical blood tests, urine, blood coagulation, RW, AIDS, hepatitis, instrumental research methods - R -graphy, CT scan of the chest, mammography, Ultrasound of the breast and zones of regional lymphatic drainage, liver. If necessary, with bone scintigraphy and MRI of the brain. The stage of the process was established on the basis of the international classification according to the TNM system (8th revision).
In all patients, the diagnosis of breast cancer was confirmed by the data of histological examination of preparations obtained during surgery or trephine biopsy of the primary tumor. Compulsory criterion The inclusion of patients in the study was IHC confirmation of TN in breast cancer, in order to obtain accurate and correct data, only those patients who were completely absent of EC and RP, as well as amplification of the Her 2/ neu protein (ER = 0, PR = 0, Her 2/ neu =0).
The sampling of tumor material for morphological study was carried out both before the start of treatment (biopsy) and after NPCT courses (operating room), which was subsequently fixed with 10-12% formalin with further preparation of the wiring according to standard methods with hematoxylin-eosin staining. The degree of malignancy was assessed based on the study of the number of tubular structures, the number of mitoses, and the severity of tumor cell polymorphism.
Radiation and clinical methods, while providing valuable information, still do not give a complete description of the OR and should be supplemented by a histological study, which, in addition to a detailed assessment of the effectiveness of therapy, significantly increases the reliability of the prognosis. The main histological parameter in assessing the TO is the volume of viable tumor elements.
It is based on taking into account changes in the overall structure of the tumor at the tissue (stroma / parenchyma ratio, structural atypia) and cellular levels (degree of dystrophy and cell polymorphism, mitotic activity). This classification distinguishes 4 degrees of OO:

- Grade I - more than 50% of the tumor parenchyma is preserved;
- II degree - 20-50% of the tumor parenchyma is preserved;
- III degree - up to 20% of the tumor parenchyma remained in the form of separate foci;
- IV degree - complete absence of tumor parenchyma.

To objectify the assessment of therapeutic pathomorphosis according to G.A. Lavnikova uses a quantitative indicator - the damage index (IP), calculated by the formula:

$$IP = Pk - Pl / Pk \times 100, \quad (1)$$

where:
PC - the average volume of viable tumor parenchyma (without treatment);
Pl - the average volume of viable tumor parenchyma (after treatment);
IP - damage index in percent (from 100 to 0).
The following formula is used to determine treatment-induced necrosis in tumor tissue:

A \u003d B / C × 100, (2)

where:
B - the number of cells in necrosis;
C is the total number of tumor cells;
A is the percentage of cells in a state of necrosis in relation to all tumor cells.
IHC study was performed on surgical and biopsy material in the department of pathomorphology City branch of RSNPMTSOiR. Immunohistochemical examination was carried out according to this technique on the basis of the diagnostic clinic Mediofarm Ltd. "PREMIUM DIAGNOSTICS". To determine the difference, four main levels of statistical significance were taken: high - p <0.001, average p<0.01, low (limiting) p<0.05, insignificant (insignificant) - p>0.05. Evaluation of receptor expression was carried out by a quantitative method, taking into account the absence of positive cells. (Fig. 2.1, 2.2, 2.3).

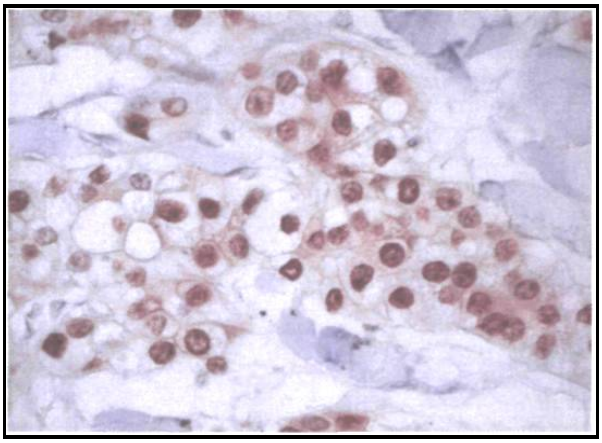


Figure 2.1. Positive IHC test for androgen receptors with TN breast cancer (magn . x 400).

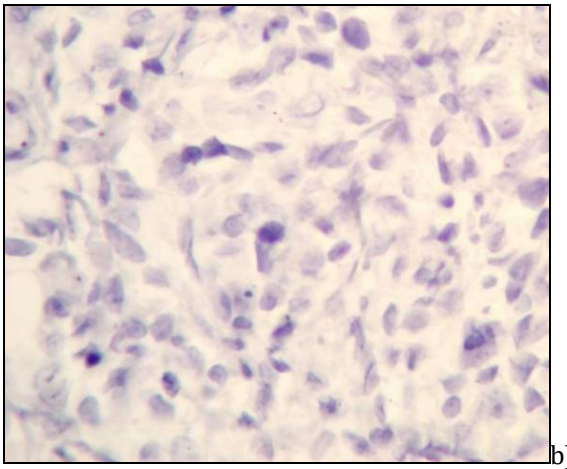
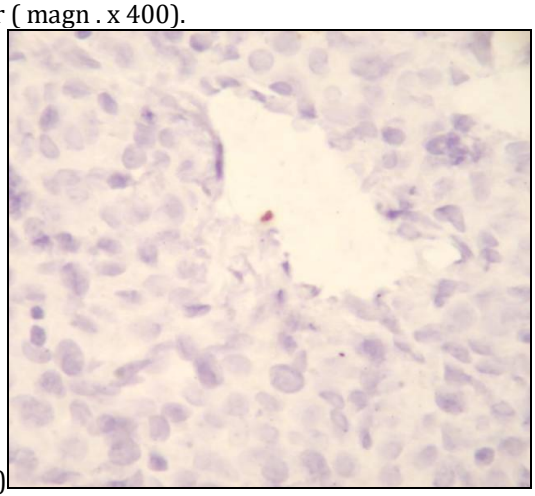
a)  b) 

Figure 2.2. Negative expression of estrogen (a) and progesterone (b) receptors in the breast. Magnification x200

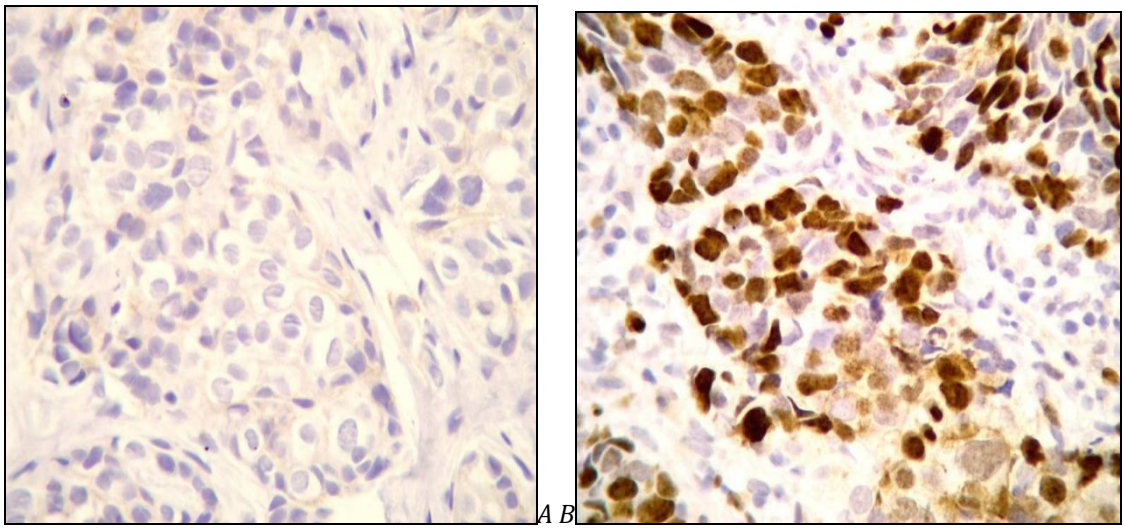

A B

Figure 2.3. Negative expression of Her-2/ neu (a) and Ki-67 (b) in breast tissue. Magnification x200

Depending on the treatment, the patients were divided into 3 groups:

Group I - 47 patients with complex therapy, including NPCT, radical surgery, radiation therapy. NPHT was carried out according to the following schemes:

a) FAC /AC/ F E C 6-courses (previously conducted scheme) (n =15),

b) AC→T cyclophosphamide + doxorubicin regimen - 4-course followed by the introduction of paclitaxel 8 times, weekly at a dose of 175 mg/m ^{2} every 3 weeks of the 3-course (the present generally accepted standard scheme) (n = 16),

c) TC or TP scheme - paclitaxel / docetaxel + carboplatin / cisplatin (docetaxel + cisplatin in edematous-infiltrative form) 1 time in 3 weeks 6 injections (suggested scheme in this study) (n = 16);

patients aged 18 to 59 years, mean age - 49 $\pm$ 0.8 years, by stages - II a - 6.4%, IIb - 25.5%, IIIa - 38.2%, IIIb - 14.8%, IIIc - 14.8%.

Group II - 43 patients with complex treatment in the amount of radical surgery, APCT and RT; in the adjuvant mode, the following chemotherapy regimens were used:

a) FAC / F E C (fluorouracil + cyclophosphamide + doxorubicin or epirubicin) (previous regimen) (n = 12);

b) AC (cyclophosphamide + doxorubicin) 4-course followed by the introduction of paclitaxel at a dose of 80 mg / m ^{2} 8 injections weekly or paclitaxel 175 mg / m ^{2} - every 3 weeks 3 courses or paclitaxel + carboplatin or docetaxel + cisplatin (for nodular form with secondary edema) up to 6-8 courses once every 3 weeks (proposed scheme in this study) (n = 15);

b) AC (cyclophosphamide + docorubicin) 4-course followed by the introduction of paclitaxel + carboplatin up to 6-8 courses 1 time in 3 weeks (the present generally accepted standard scheme) (n = 16);

The age of patients was 45-59 years, the average age was 45.7 $\pm$ 0.6 years, by stages: I - IIa - 37.2 %, IIb - 34.8%, IIIa - 11.6%, IIIb - 9.3 %, IIIc – 6.9%.

Group III - 34 patients with TN breast cancer who received complex treatment - NPCT, radical surgery, radiation therapy.

The NPCT regimen was as follows: TC or TP - paclitaxel / docetaxel + carboplatin / cisplatin (docetaxel + cisplatin for nodular form with secondary edema) 1 time in 3 weeks for 6-8 courses. After complex therapy according to the above scheme, treatment continues with monotherapy. capecitabine (up to 6 courses) (suggested regimen in this study) (n =34);

The age had a uniform distribution, the patients were predominantly young up to 46 years old and over 45-50 years old, which accounted for 40%, the distribution by stages was as follows: IIa - 8.8 %, IIb - 38.2%, IIIa - 38.2%, IIIb - 8.8%, IIIc - 5.8%. All groups taken for the study were comparable in terms of the main prognostic factors: age, general condition, the extent of the tumor process. As can be seen from table 3.1. depending on age, the majority of patients were aged 35-54 years, i.e. relatively young, with the largest number of them being at the age of 45-54 years, which amounted to 32.5%, slightly less - at the age of 35-44 years - 30.1%, respectively.

According to the menstrual status, patients in perimenopause prevailed - 42.9%, while there were no patients in postmenopause. Most patients had 3 or more pregnancies - 47.6%, and when studying the presence of the BRCA mutation - in an equal percentage, it was characterized by both the presence and absence (14.0 and 14.3%, respectively, while in 72.2 % of patients, it was not determined. According to

the main indicators of prognostic value, such as the size of the tumor, most of them were characterized by an average of 2 to 5 cm, which amounted to 46.1%, it should also be noted the complete absence, or a small size up to 2 cm - was determined in 19%, large tumors - from 5 to 10 cm were found only in 9.5% of patients.

According to the presence of l / y in most patients (70.6%), axillary ones were determined, and subclavian and supraclavicular ones were absent in 63.5 and 85.7% of patients, respectively. In contrast to the data of foreign researchers, in the analyzed group of patients with TN breast cancer, more often than in other subtypes, there was a clinically detectable lesion of the axillary (in 70.6% of cases), subclavian (36.5%) and supraclavicular (14.3%) l / y, which led to a total high incidence of locally advanced tumors in TN BC (stages IIb - III c - 75.4%). This may be due to the more aggressive course of the disease and the rapid progression of the tumor, given its biological subtype.

Ductal cancer was the most common - 66.7%, the least - apocrine and metaplastic types, 5.6 and 1.6%, respectively, while invasive lobular and medullary occurred, respectively, in 11.1 and 15.1 % of patients. As noted earlier, according to the degree of malignancy, the patients had mainly 2nd and 3rd degrees - 66.7 and 33.3%, respectively. According to the definitions of the expression of estrogen receptors, progesterone and the HER-2/ neu gene in all patients, it was negative, which confirmed the diagnosis of TN in all patients included in the study. The study of the expression of Ki -67 showed its high activity up to 80-95%, which indicates a high proliferative activity of this type of tumor and an aggressive course of the process, contributing to an unfavorable outcome of the disease.

The analysis of the history data showed that in the vast majority of cases (89.8%), the patients themselves detected the presence of a node in the breast, and in some cases noted its rapid growth. Sometimes the tumor was an accidental finding detected during a medical examination.

When conducting clinical examinations on mammograms, nodes of various shapes were usually visualized, often with jagged edges. Microcalcifications were relatively rare and were not typical - up to 8% of cases. When studying mammograms in patients in the study groups, it was not possible to identify the absence of background processes in the breast tissue surrounding the tumor, although some regard them as a pathognomonic sign of breast cancer TN.

During ultrasound, the tumors looked like hypoechoic structures with increased vascularization, the presence of cysts of different sizes was noted, with strands along the anterior contour, in some cases with a “path” to the nipple. For the purpose of primary verification of the diagnosis in half of the cases (46.0%), the method of trephine biopsy was used, followed by histological examination of the material, in 38.0% of cases the diagnosis of breast cancer was made according to the results of the first puncture, in 5 cases - after the second puncture of the breast. In two cases, only a suspicion of the presence of breast cancer was expressed, in another 2 - the answer was uncertain and in one case it turned out to be false negative. Another false-negative response was obtained in the study of discharge from the nipple, however, it should be clarified that in this patient the source of the discharge was cystic structures adjacent to the solid component of the tumor, and essentially could not contain tumor cells.

In 72.2% of cases, primary verification of TN in breast cancer was carried out based on the findings of a trephine biopsy, and subsequently an additional IHC study of the material was carried out in order to confirm TN in breast cancer. 12 (9.5%) patients were admitted to the clinic with a verified diagnosis of breast cancer, after therapeutic measures (3 patients after prolonged use of non-traditional therapies). At the same time, the reason for the treatment of patients in a specialized institution was the lack of effect after the therapy.

According to the localization of the tumor in 56.3% of cases, the tumor was located in the left, and in 41.3% - in the right breast. We observed metachronous bilateral lesions only in 2 patients (1.6%), synchronous (0.8%) - in 1 patient, in 1 patient the clinical process was initially erroneously regarded as metachronous cancer, because the interval of its detection in another MF was extremely short.

On the border of the outer quadrants, the tumor was localized in 53 patients, in the inner quadrants in 11, in the central sections - in 18 patients. At the same time, 12 patients had a multicentric form of tumor growth, 23 had the disease manifested by clinical symptoms of an edematous-infiltrative form, necrosis with ulceration of the tumor - in 5. The majority of patients in this group were young and middle- aged patients (30-50 years old - 59 ,1% and 50 -60 years old 23.8%), having a somatic status according to ECOG 1-2 points.

All patients underwent surgery, depending on the subsequent chemotherapy regimens, they were divided into 3 groups (Fig. 2.3):

group 1 - 47 patients who received NPCT with a radical operation and RT according to the standard method;

group 2 - 43 patients who underwent radical surgery with APCT and RT according to the standard method;
group 3 - 34 patients who received NPCT with a radical operation and RT according to the standard method, followed by the appointment of monochemotherapy capecitabine.
Patients (n = 124) underwent surgical interventions in various volumes: radical resection (RR) - 28 (22.5%); radical mastectomy (RME) - 78 (62.3%), skin- sparing or subcutaneous mastectomy with reconstruction with an expander and subsequent replacement of the expander with an implant - 4 (3.2%), simple mastectomy - 3 (2.4%), except for 2 (1.6%) patients who did not undergo intervention due to the presence of a severe concomitant disease. In 4 patients, skin- sparing or subcutaneous mastectomy with expander reconstruction was performed; after RT, the second stage of breast reconstruction was performed - replacement of the expander with an implant. 2 patients underwent prophylactic subcutaneous mastectomy with simultaneous reconstruction with an implant. In the postoperative period, patients received treatment according to the standards. During the surgical stage of treatment among 124 patients with TN in the postoperative period, complications were noted, primarily due to the volume of surgical interventions performed, so in 18 (14.5%) cases, the development of lymphostasis of the upper limb was recorded; in 13 (10.5%) - prolonged lymphorrhea; in 1 (0.8%) case – marginal necrosis of the flap (after RME), as a result of which the healing of the postoperative wound was partially due to secondary intention.
In the course of the study, an analysis was made of the presence of a family oncological history by studying the case histories and interviewing patients. According to the survey, cases of familial breast cancer were identified in 11 (12.5%) patients. At the same time, in 3 patients, o to breast cancer occurred among mothers, in 1 patient, the mother had verified o van bilateral breast cancer, in 2 - breast cancer, o was determined in grandmothers on the mother 's side, in 1 - and in m a teri , and y b a bushes ; in 3 cases - breast cancer was verified in mother's sisters , in 3 cases - in father's sisters (6 cases).
It should also be noted that the patients were determined aggravated o nc o gynecological a anamnesis. So, in 2 patients, the mothers suffered from endometrial cancer, in 2 patients, a diagnosis of primary multiple cancer - breast cancer and endometrial cancer was diagnosed. In 3 cases, aunts and two sisters of the patient were ill with cancer. Ovarian cancer (OC) was noted only in 1 case in the mother of the patient, in 1 - R a to the vulva, in the grandmothers of the bushes of 2 patients on the mother 's side in amnesa verified cervical cancer. Attention should be paid to the presence among the relatives of patients , while the female line showed a tendency to damage the gastrointestinal tract: in 3 patients from the maternal line, there were cases of stomach cancer (GC), pancreas (PC) and cancer easy ogo (RL) (1 observation); in 2 - cancer of the food o yes (RP) in the grandmother on the maternal side, 1 - cancer of the sigmoid colon in the grandmother on the paternal line and 1 - primary liver cancer in the sister otc .
According to the male or odcoconoyline, c b was detected: prostate cancer in 2 patients occostoro us o tc a; RL - the father of 1 patient and the paternal grandfather. In 1 patient, onko logical pathology was a o b o their grandfathers - at od ogo - RTC, at a friend ogo - RP. The uncles of one patient (it was not possible to detail the family line) suffered from cancer of the throat (WG).
Thus, the most characteristic feature of breast cancer, which is hereditary, is the cumulation of oncological diseases within the family (among blood relatives of the I–II degree of kinship). In the course of a survey of patients and a retrospective study of primary documentation, a high incidence of a combination of breast cancer and OC in blood relatives of patients was revealed.
According to the histological type of breast cancer TN, they were distributed as follows: 84 cases (67.7%) - invasive ductal cancer (nonspecific type (NST), 12 (9.7%) - invasive lobular cancer, 17 (13.7%) - medullary cancer, 7 (5.6%) - apocrine cancer, 2 (1.6%) - metaplastic (Fig. 3.5) .Thus, the ratio of different histological types of TN in breast cancer did not contradict and was consistent with similar WHO data [WHO , 2012].
According to According to the schemes and modes of chemotherapy used, the patients were divided into the following groups:
Group I - 47 patients with complex therapy, including NPCT, radical surgery, radiation therapy. NPHT was carried out according to the following schemes:
a) FAC /AC/ F E C 6-courses (previously conducted scheme) (n =15),
b) AC→T cyclophosphamide + doxorubicin regimen - 4-course followed by the introduction of paclitaxel 8 times, weekly at a dose of 175 mg/m ^{2} every 3 weeks of the 3-course (the present generally accepted standard scheme) (n = 16),
c) TC or TR scheme - paclitaxel / docetaxel + carboplatin / cisplatin (docetaxel + cisplatin in edematous-infiltrative form) 1 time in 3 weeks 6 injections (suggested scheme in this study) (n = 16);
patients aged 18 to 59 years, mean age - 49 $\pm$ 0.8 years, by stages - II a - 6.4%, IIb - 25.5%, IIIa - 38.2%, IIIb - 14.8%, IIIc - 14.8% with 1-2 points of assessment of somatic status according to ECOG.

In this group of patients, the choice of the chemotherapeutic scheme was carried out taking into account international recommendations (ESMO and ASCO). The average number of NPCT courses received by patients was 5.36 ± 1.14 (from 2 to 8) courses. Dose reduction was required in 14 patients. The majority (58.2%) of patients in this group of TN in breast cancer had at the time of detection II b - IIIc stage of the disease. In most cases, TN breast cancer was an infiltrating ductal carcinoma of a nonspecific type (62.7%) of the third degree of histological malignancy.

Before the start of NPCT, all patients underwent a biopsy from the tumor tissue for histological verification of invasive breast cancer and obtaining data on the presence/absence of ER, RP, and HER -2 expression. The choice of chemotherapy regimen was carried out according to the existing standards (or ongoing research) of the clinic at the time of treatment. Evaluation of the effectiveness of therapy was carried out on the basis of clinical examination, ultrasound, R -graphy or CT (according to RECIST 1.0 criteria), which was carried out after every 2-3 courses of treatment. The safety of the treatment was assessed according to the standards of severity of clinical manifestations.

Group II - 43 patients with complex treatment in the amount of radical surgery, APCT and RT; in the adjuvant mode, the following chemotherapy regimens were used:

a) FAC / F E C (fluorouracil + cyclophosphamide + doxorubicin or epirubicin) (previous regimen) (n = 12);

b) AC → T (cyclophosphamide + doxorubicin) 4-course followed by the introduction of paclitaxel at a dose of 80 mg / m^2 8 injections weekly or paclitaxel 175 mg / m^2 - every 3 weeks 3 courses or paclitaxel + carboplatin or docetaxel + cisplatin (for nodular form with secondary edema) up to 6-8 courses once every 3 weeks (proposed scheme in this study) (n = 15);

b) AC→TC (cyclophosphamide + docorubicin) 4-course followed by the introduction of paclitaxel + carboplatin up to 6-8 courses 1 time in 3 weeks (the present generally accepted standard regimen) (n = 16);

The second group included patients predominantly aged 45 to 59 years (mean age - 45.7 ± 0.6 years) Fig. 3.7, with 0-1 score of somatic status according to ECOG (68.8%). The majority (31.2%) of patients in this group of TN BC had stage I-IIa of the disease at the time of detection. According to the morphological type, characteristic tumors were ductal carcinoma (75.0%), mainly in the third degree of histological malignancy (more than 60.0%).

Analysis of the distribution of patients with breast cancer by stages of the process included in this group showed that there was a quantitative advantage of patients in II a - 9.3% and III c - 7.0% stages. This is due to the detection in the postoperative material obtained from these patients of metastases in the subclavian lymph nodes (axillary lymph nodes III level, N_3), which were often not clinically diagnosed in the preoperative period. This confirms that subtypes of TN in breast cancer are more aggressive compared to other types of tumors. The following chemotherapy regimens were used in the adjuvant regimen: FAC / F E C (fluorouracil + cyclophosphamide + doxorubicin or epirubicin) or AC (cyclophosphamide + doxorubicin) 4-course followed by paclitaxel at a dose of 80 mg / m^2 8 injections weekly or paclitaxel at a dose of 80 mg /m^2 8 injections weekly or paclitaxel 175 mg/m^2 - every 3 weeks 3 courses (n=16) or Paclitaxel + carboplatin or docetaxel + cisplatin (with edematous-infiltrative form) up to 6-8 courses 1 time in 3 weeks (n= 12); AS (cyclophosphamide + docorubicin) 4-course followed by the introduction of paclitaxel + carboplatin up to 6-8 courses 1 time in 3 weeks (n=15) (Table 3.4).

Group III - 34 patients with TN breast cancer who received complex treatment - NPCT, radical surgery, radiation therapy.

The NPCT regimen was as follows: TS or TR - paclitaxel / docetaxel + carboplatin / cisplatin (docetaxel + cisplatin for nodular form with secondary edema) 1 time in 3 weeks for 6-8 courses. After complex therapy according to the above scheme, treatment continues with monotherapy. capecitabine (up to 6 courses) (proposed regimen in this study); (tab. 3.5).

In this group, the age of patients had a uniform distribution, i.e. there was an advantage in younger patients up to 46 years and older (18-44, 45-59 years - 40%. At the same time, most patients were in stage IIa , IIb and IIIa - 12 - 16%. According to the degree of histological malignancy, most patients were in 3rd stage (64.4%). Moreover, according to the morphological type of the tumor, the ductal variant was the most characteristic more than 60%

RESULTS AND DISCUSSION

Currently, CT is actively used in the neoadjuvant regimen in the treatment of patients with TN in breast cancer, as it allows to reduce the size of the primary tumor, which helps to achieve an increase in the number of organ- preserving operations performed while maintaining a cosmetic result. It also allows assessing the sensitivity of the tumor to the treatment in a short period of time. It should be noted that

the verification of TN in breast cancer determines the inefficiency of such targeted treatment regimens, both hormone therapy and targeted therapy with Herceptin, which leads to the search for effective chemotherapy regimens that provide complete morphological regression of the tumor (TMR), which have important prognostic value as a criterion for evaluating NAC.
In this study, the evaluation of the effectiveness of NAC in patients with TN breast cancer was carried out using the analysis of the frequency of complete morphological regressions.
Grade efficiency NHT was carried out on the foundation _ results control surveys (mammography and ultrasonic study mammary glands, axillary, supraclavicular and subclavian lymph nodes) and data about degrees medical pathomorphosis tumors obtained as a result of histological examination of the surgical material.

Table 3.3: The frequency of achieving complete therapeutic pathomorphosis in tumors and lymph nodes

Complete pathomorphosis	FAC / AC (n =27)	TC(DC) (n =16)	AC →T (n =15)
In a tumor	14.7%	63%	44.7%
In the tumor and in the l/n	14.7%	55.6%	40.8%

Depending on the NPCT regimens used, when analyzing the frequency of achieving complete therapeutic pathomorphosis , which was studied both in the tumor and in the l / y, it showed that the most effective was the TS(DC) regimen, in which pathomorphosis in the tumor was achieved in 63%, and in the tumor and l / y 55.6%, respectively. When using the FAC / AC and AC → T NPCT regimens, it was the least observed in equal shares of 14.7% with the FAC / AC regimen, which is relatively large 44.7% in the tumor, 40.8% in the tumor and l / y with the regimen AC → T. Evaluation of the effectiveness of NAC showed that 22 (46.8%) female patients on the background carried out CT was achieved complete regression of the tumor (therapeutic pathomorphosis IV degree); in 12 (25.5%) - partial regression (pathomorphosis III degree); in 9 (19.1%) - stabilization (pathomorphosis II degrees), in 4 (8.5 %) patients noted progression disease (pathomorphosis) I degree) (Fig. 3.8)

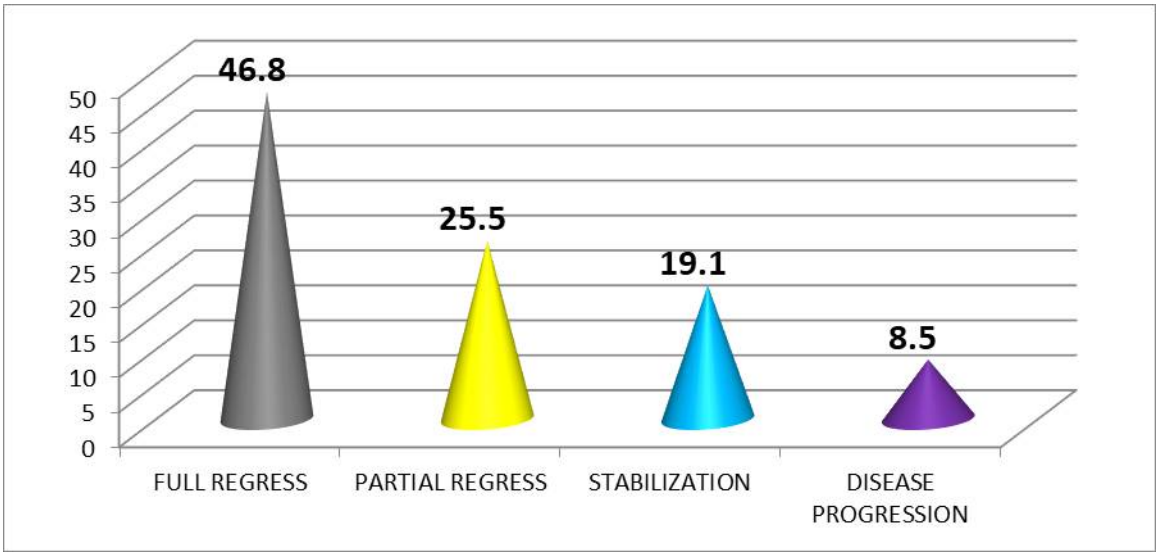


Figure 3.8. Evaluation of the effectiveness of NPHT in the study groups according to the degree of pathomorphosis

When assessing the frequency and completeness of the achieved therapeutic effects, depending on the NPCT regimens used in the study groups, the following results were obtained (Table 3.4).

Table 3.4: Evaluation of the achieved therapeutic effect of NPCT (therapeutic path morphosis)

Therapeutic pathomorphosis	FAC / AC / E C n =16		TC or DC 3-week or weekly n =16		AC→T n =15	
	abs.	%	abs.	%	abs	%
Complete regression, n= 22	3	18.7	fifteen	93.7	four	26.6
Partial regression, n= 12	four	25.0	one	6.2	7	46.6
Partial regression/stabilization, n= 9	6	37.5	-	-	3	20.0
No effect, n= 4	3	18.7	-	-	one	6.7

As can be seen from Table 3.4, in patients treated with NPCT according to the TC regimen, the frequency of achieving complete pathomorphological regression was significantly higher (93.7%) than in patients using the FAC (18.7%) or AC → T (26. 6%).

Table 3.5: Evaluation of the effectiveness of treatment in edematous-infiltrative form Breast cancer with NPCT

Therapeutic Pathomorphosis	docetaxel + cisplatin every 3 weeks (n =13)		paclitaxel + carboplatin every 3 weeks. or weekly (n =12)	
	abs.	%	abs.	%
Complete regression	ten	76.9	5	41.7
Partial regression	3	23.1	four	33.3
Partial regression/stabilization	-	-	2	16.6
no effect	-	-	one	8.3

The study of the NPCT regimens used in the edematous-infiltrative form showed low efficiency, but the use of docetaxel with cisplatin contributed to an increase in the response rate to chemotherapy, while complete pathomorphological regression was significantly higher (78.6%) than in patients treated with paclitaxel and carboplatin (tab. 3.5).

In addition to evaluating the effectiveness of NCT, an analysis of its side effects, which occurred in all patients, was carried out.

The main negative manifestations of the impact were hematological toxicity - leukopenia and thrombocytopenia, nausea, vomiting, stomatitis, hand-foot syndrome, etc. The above side effects required corrective symptomatic therapy, but did not lead to a delay or cancellation of treatment (Table 3.1).

Table 3.6: Toxic reactions of studied NPCT regimens (n =47)

Scheme NPHT	Leukopenia	thrombocytopenia	nausea, vomit	stomatitis	diarrhea	other
CAF / FAC /AC every 3 weeks	9 (19.1)	2 (4.2)	ten (21.2)	2 (4.2)	2 (4.2)	one (2.1)
TR or TS in 3-weeks or weekly	6 (12.7)	one (2.1)	one (2.1)	2 (4.2)	6 (12.7)	7 (14.9)
AC →T every 3 weeks	9 (19.1)	one (2.1)	5 (10.6)	3 (6.3)	four (8.5)	four (8.5)
Total	24 (51.1)	four (8.5)	16 (34.0)	7 (14.9)	12 (25.5)	12 (25.5)

CAF / FAC / AC and AC → T regimens were the most toxic, with manifestations of hematotoxicity (19.1% - leukopenia; 4.2 - thrombocytopenia), among other symptoms, nausea and vomiting were the most common 34.0 %.

APCT was performed in 36 patients with TN in breast cancer, 5 of them had previously received NPCT (according to the FAC / AC / EC scheme) for IIb - IIIc stages of the disease. Only APCT received 31 (86.1%) patients, more than 2/3 of them received anthracycline -containing regimens as APCT, Monotherapy taxane- containing drugs (n = 8) , 24 (13.3%) - anthracyclines and taxanes , another 5 (2.8%) patients received not containing anthracyclines , a combination of platinum and taxanes .

When evaluating the effectiveness of APCT, its side effects were analyzed, which were noted in all patients. The main manifestations were hematological toxicity (leukopenia and thrombocytopenia), nausea, vomiting, stomatitis, hand and foot syndrome, etc. (Table 3.7).

Table 3.7.Toxic reactions of APCT (n= 31)

APHT scheme	Leukopenia	thrombocytopenia	nausea , vomit	Stomatitis	diarrhea	other
AC→T, weekly or in 3 weeks 1 time	8 (2 5, 8)	1 (3.2)	7 (22.5)	1 (3.2)	2 (6.5)	1 (3.2)
TA in 3 weeks 1 time	9 (29.0)	2 (6.5)	4 (12.9)	7 (22.5)	4 (12.9)	3 (9.7)
AC→TC weekly or 3 weeks 1 time	7 (22.5)	1 (3.2)	3 (9.7)	1 (3.2)	1 (3.2)	1 (3.2)
Total	24 (77.4)	4 (12.9)	14 (45.2)	9 (29.0)	7 (22.6)	5 (16.1)

During APCT, hematological toxicity of 77.4% was also noted, which was mainly characterized by leukopenia and occurred in equal proportions with all the schemes used; nausea and vomiting were typical for 45.2% of patients, which was most pronounced with AC → T regimen of chemotherapy treatment (22.5%).

During chemotherapy courses in patients with TN in breast cancer, despite the existing toxicity of chemotherapy drugs, it was possible to stop it with the use of accompanying therapy carried out to correct emerging complications. The effectiveness of the treatment is assessed by studying the overall and relapse -free survival of patients. In this work, the 3rd and 5th survival rates of patients with TN in breast cancer were studied. The study of the survival of patients depending on the histological type of TNBC showed that the five-year DFS with invasive lobular cancer was 49.5 ± 6.4%, with nonspecific - 79.8 + 3.7%, with medullary and apocrine variants - 81 , 4±3.6 and 82.2±2.7 ($p<0.05$).

An analysis of the five-year OS showed that it was 79.2±3.9% for the invasive nonspecific type , and 62.5±17.6% for the invasive lobular type ($p<0.05$). With a more aggressive histological form of the metaplastic subtype, an unfavorable prognosis is noted, while the three-year DFS was 43.4±3.2%, OS 38.2±3.9%, and there were no cases of five-year OS. With a more aggressive histological form of the metaplastic subtype (n = 2) , an unfavorable prognosis was noted, while the 3-year DFS was 43.4 + 3.2% and OS 38.2 + 3.9%, 5-year OS in none of the patients not found. Patients with medullary and apocrine TN breast cancer (n = 7) showed no signs of disease progression and had a 97% 5-year OS.

Thus, patients with medullary and apocrine variants of the morphological structure of the tumor have a more favorable prognosis than other subtypes of TN in breast cancer. The analysis of DFS and OS revealed statistically significant differences between the studied subgroups of patients: patients with TN breast cancer had the worst prognosis. An important indicator of the effectiveness of NPCT, which determines the possibility of surgical treatment, is the achievement of complete pathomorphological regression.

The best results were achieved in patients receiving platinum and taxane -containing drugs, so (DC - docetaxel + cisplatin in the edematous-infiltrative form), regardless of the degree of histopathological differentiation. With the third degree of tumor differentiation (G 3), complete pathomorphological regression could not be achieved when using chemotherapy according to the FAC /AC/EC and AC→T schemes.

One of the main tasks that we faced was to evaluate the long-term results of NPCT in patients with TN in breast cancer. Thus, we considered the 5-year DFS depending on several indicators, one of which was the determination of the degree of achievement of pathomorphological regression.

In the absence of therapeutic pathomorphosis of the tumor after NPCT, patients had a relapse of the disease during the first year after treatment, regardless of its continuation. By the third year of the study, the manifestation of the disease was observed in all patients. In patients with “stabilization” and “partial regression”, the 5-year DFS was 65.2% and 67.6%, respectively ($p<0.05$), in the subgroup with achieved complete pathomorphosis , the 5-year DFS was 79.9 % ($p<0.05$).

According to the data of the present study, the treatment option had a significant effect on DFS ($p = 0.029$) and OS ($p = 0.037$): optimal long-term results were achieved with NPCT using a combination of platinum and taxanes , while with the use of anthracycline drugs , the worst prognosis, because long-term results are inferior to the standard regimens used (Fig. 3.10).

According to our study, the achievement of complete therapeutic pathomorphosis was associated with improved survival in the subgroup in which patients received NPCT with TR or DP preparations: 5-year DFS among patients who achieved complete therapeutic pathomorphosis was 81.8 ± 6.0% ($p<0.05$).

However, taking into account the data on the unequal survival of patients who received various platinum-containing regimens with an equally high frequency of achieving complete therapeutic pathomorphosis,

and a higher survival rate of patients from the AC / T group than in the AC group, it becomes obvious that complete therapeutic pathomorphosis is not always correlates with improved long-term outcomes of treatment. In this regard, the decision to adapt new regimens of APCT and NPCT on the basis of an increase in the frequency of achieving a complete therapeutic pathomorphosis must be made with caution. The APCT regimen had no significant effect on either DFS or OS ($p < 0.05$).

The results obtained, on the one hand, confirm the high activity of platinum-containing regimens, but it should be noted that the choice of a partner drug is important, which requires additional research for the widespread introduction of platinum-containing regimens into clinical practice.

In order to identify the optimal time for the use of drug therapy, we compared the results of APCT and NPCT in patients with early (I - IIa) and conditionally operable (IIb- IIIa) stages of the disease.

The survival of patients did not statistically significantly differ depending on the time of receiving drug treatment, either in early ($p = 0.26$ for DFS and $p = 0.683$ for OS) or conditionally operable stages of the disease ($p = 0.141$ for DFS and $p = 0.101$ for OS), however, in the latter, in numerical terms, there was a clear tendency to worsen DFS and OS when using APCT (Table 3.8).

Table 3.8. 5-year DFS and OV primary operable patients, depending on the conduct of APCT and NPCT

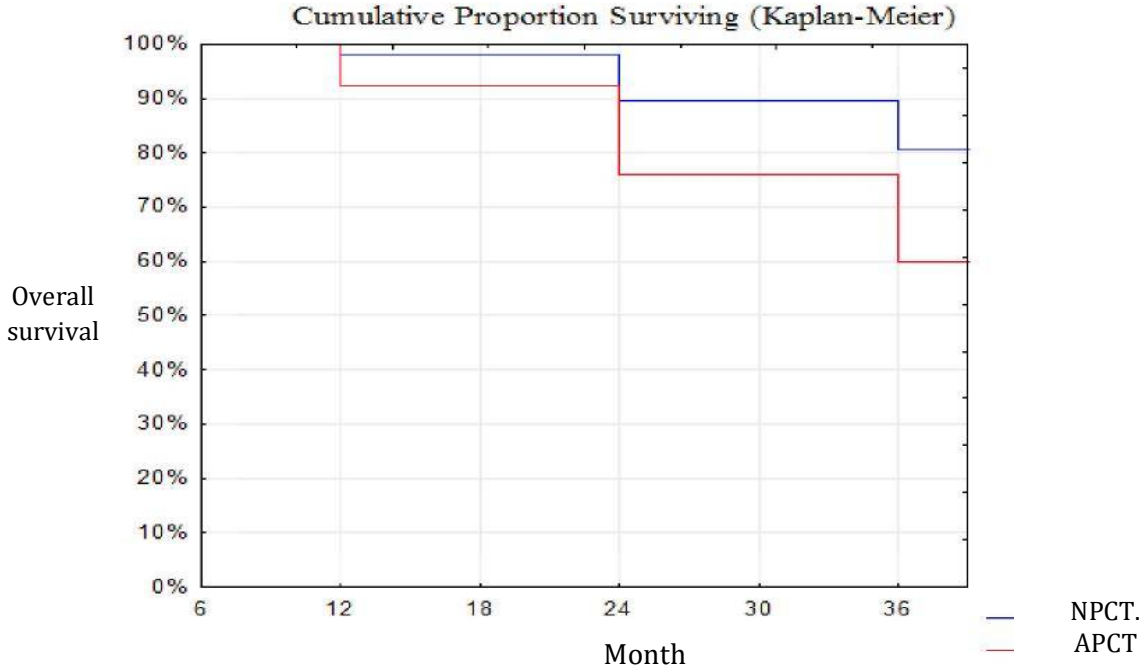
Chemotherapy option	5 year old I - II a Art. (%)		5-year-old at IIb - IIIa Art . (%)	
	DFS	OS	DFS	OS
NPHT	91.0+3.6	81.3+3.8	84.0+7.6	77.1+2.9
APHT	77.3+8.9*	62.3+3.3	72.0+8.1*	61.2+6.3*

Note: * $p < 0.05$ significance of differences with the data of the group of patients treated with NPHT

Thus, the data obtained indicate the equivalence of APCT and NPCT in patients with resectable stages of TN BC and the need for their careful use in NPCT in patients with more common, but initially resectable tumors. 5-year OS in the compared groups was expectedly better in patients who underwent NPCT.

After neoadjuvant treatment, OS rates approached 81% ($p < 0.05$), while with antihypertensive chemotherapy it was 62%. DFS in the NPCT group was 74.6% ($p < 0.05$), without it - 40.7% ($p < 0.05$). The obtained data give grounds to assert that the appointment of neoadjuvant cytotoxic therapy significantly increases the parameters of the DFS and OS in patients with TN in breast cancer.

An analysis of survival depending on clinical stages showed that the results of the treatment performed depend on the spread of the process: In these, primary o respectable stages, the survival of patients is satisfactory and comparable with other subtypes of breast cancer, a significant decrease in the rates of OS and DFS is observed with conditionally - o respectable process ($p < 0.001$) (Fig. 3.12).



Rice. 3.12 5-year RH by intervention chemotherapy treatment

Application of taxanes is preferred how when planning neoadjuvant treatment, and during adjuvant therapy. It is also necessary to emphasize the fact that anthracyclines do not lose their relevance in the treatment of TN in breast cancer and can be used in the above regimens.

This is due to the high risk of micrometastases in patients and the low efficiency of systemic treatment of TN in breast cancer at the present time. The 3-year OS in the compared groups was significantly higher among patients who underwent NPCT, so OS in this case approached 80%, while with APCT it was 60%.5 year old OV amounted to :at I st. - 89.7 % , IIa - 84.5 %, II b - 77.8 %, IIIa - 53.3 %, III b - 45.4%, Sh c - 24.0%. 5 year old BRV at patients who received complex treatment forabout TNBC, amounted to: at I Art. – 90.9%, II a - 85.9% IIb _ - 80.3%, III a - 48.9%, III b - 53.9%, III c - 45.1% (p <0.001) patients. Death in the first year of observation was recorded in 1 (0.8%) case. The efficacy and safety of combinations of various chemotherapy regimens followed by continued treatment in monotherapy with capecitabine as a treatment for TN in breast cancer is undeniable. The data obtained show that the addition of capecitabine after the use of systemic chemotherapy leads to an increase in median progression-free survival (compared with chemotherapy alone) from 36.7 to 27.9 months (p <0.001) (Table 3.9).

Table 3.9:The effectiveness of the combination of capecitabine with chemotherapy

Goals	complex treatment with capecitabine up to 6 courses (n = 36)	complex treatment without capecitabine (n =83)	R
Immediate efficiency, %	39.5	29.6	<0.001
Median time to progression, months	36.7±3.9	27.2±4.3	<0.05
5-year survival, %	84.6	81.5	<0.01
Median overall survival, months	49.7±3.4	36.4±1.7	<0.001

5-year OS was statistically significantly higher in the group of patients treated with capecitabine - 84.6% compared with the control group of 81.5% (p <0.001). When analyzing the safety of new, not typical for the used drugs, no adverse events were noted. The addition of capecitabine after chemotherapy regimens in patients with TN breast cancer led to a significant increase in the frequency of DFS and OS. The results confirmed that the effectiveness of the combination of capecitabine after systemic polychemotherapy in patients with TN in breast cancer was significantly higher compared to systemic chemotherapy alone.

CONCLUSIONS

In our study, we conducted a retrospective study of the case histories of patients with TN breast cancer with the following characteristics: mean age 49±8.5 years; histopathological differentiation of the tumor - G-3; with the definition of tumor subtypes, which is the main criterion for an unfavorable prognosis of TN in breast cancer. As you know, the main indicators of the work of the oncological service are data on disease -free survival. In this work, the OS and DFS of patients were assessed, while progression in the next 5 years was determined both after NPCT and in other groups with APCT.

When analyzing the direct effectiveness of using standard PCT regimens, it was found that the incidence of complete pathomorphological regressions was significantly higher - 43.4% in the group of patients treated with taxane and platinum than in neoadjuvant treatment, which included AC, FAC or TA regimens - 6.5 % and 4.5%, respectively.

As mentioned above, the second factor causing unsatisfactory results in the treatment of TN in breast cancer is most likely the lack of available therapies for this tumor subtype. Before the advent of targeted therapy, all patients with breast cancer received only chemotherapy, which acts only on rapidly dividing tumor cells of highly aggressive subtypes of breast cancer, while the survival of other patients was due not so much to therapy as to the biological characteristics of the tumor.

The performed analysis confirmed the information of the majority of published foreign studies that the most common histological type of tumors with a triple negative phenotype was invasive ductal carcinoma. Tumors of the third degree of histopathological differentiation were much more common and accounted for 59.4% of all tumors of this subtype. A study of the survival of patients showed that the 5-year DFS with invasive lobular cancer was 49.5+6.4% compared with the nonspecific variant - 79.8+3.7%, medullary - 88.2+2.7%. Similar differences were noted in the analysis of 5-year OS: 73.2+3.9% for the invasive nonspecific type and 62.5+17.6% for the invasive lobular type, respectively. The most aggressive histological form is the metaplastic subtype, which has a poor prognosis, with a 3-year DFS of 43.4+3.2%, OS of 38.2+3.9%, no patient survived more than 5 years. In the medullary and apocrine subtypes, as shown by the analysis of signs of disease progression, no signs of disease progression were noted, and the 5-year OS was 97%.

The incidence of complete pathomorphological regressions after NCT was significantly higher in the group of patients treated with the inclusion of taxane drugs and amounted to 43.4%, according to the TC scheme - 61.8%, according to the FAC or AC→T scheme - 19.1%.

Optimal long-term results of treatment were achieved with the use of NPCT - a combination of platinum and taxanes , while combinations of anthracyclines had the worst result, yielding to standard chemotherapy regimens in terms of long-term results. On the one hand, the obtained results confirm the high activity of platinum - containing regimens, on the other hand, they indicate the importance of choosing a partner drug, as well as the need for additional studies to study the morphological subtypes of the tumor for the subsequent use of platinum -containing regimens and their introduction into wide clinical practice. In the edematous-infiltrative form, the best results were shown by the Docetaxel with Cisplatin regimen, in which the complete pathomorphological regression was significantly higher (78.6%) than in the subgroup of patients treated with paclitaxel with carboplatin or according to the standard AC regimen.

The use of taxanes is preferred as in planning neoadjuvant treatment, and during adjuvant therapy. We consider it our duty to emphasize the fact that anthracyclines have not lost their relevance in the treatment of TNBC and can be used in these regimens. The use of NPCT improved OS indicators, which amounted to 81%, the use of APCT - 62%, DFS with NPHT - 74.6%, without NPHT - 40.7%. The APCT regimen did not have a significant effect on the DFS and OS, which determines the need for the use of NPCT in TN in breast cancer. This data confirms that the appointment of neoadjuvant cytotoxic therapy significantly increases the rates of DFS and OS in patients. The appointment of neoadjuvant cytotoxic therapy significantly increases the rates of DFS and OS in patients with TNBC. The best results were achieved in patients receiving platinum with taxane. containing regimen, regardless of the degree of histopathological differentiation and stage of the disease. Administration of capecitabine monotherapy after SCT increased median progression-free survival (compared to chemotherapy alone) from 46.7 to 49.2 months, improving 5-year OS to -84.6% versus 81.5%.

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