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Individualized Treatment Planning For Breast Cancer With Lung Metastases, Incorporating Prognostic Factors

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Abstract: Currently, breast cancer is one of the five most common oncological diseases in the world and is the leading cause of death among women under 50 years of age. Purpose of the study. Improving the effectiveness of treatment of breast cancer with metastases to the lungs by differentiated use of antitumor therapy methods based on the prediction of metastasis to the lungs and three-year survival. Material and methods. Planned study of 60 case histories of ER+ PR+ breast cancer with metastases to the lungs. Result. The

prognosis of ER+ PR+ breast cancer with metastatic lung involvement was studied using multivariate analysis].

Key words: Breast cancer, estrogen, progesterone, Her2neu, CDK4, prognostic factors

Introduction: Background. Breast cancer occurs worldwide in women of all ages after puberty, with incidence rates increasing with age. Estimates show striking disparities in the burden of breast cancer in different countries depending on the level of human development [4,7,9]. In 2022, breast cancer was diagnosed in 2.3 million women and caused 670,000 deaths worldwide. Thus, in countries with a very high Human Development Index (HDI), breast cancer is diagnosed in every 12th woman during her lifetime, and it causes death in every 71st woman [6,12,15]. On the other hand, in countries with a low HDI, breast cancer is diagnosed in only every 27th woman during her lifetime, but it causes death in every 48th woman. Breast cancer metastasis is a major and challenging problem in oncomammology [13]. Metastatic breast cancer remains a critical challenge in oncology. It ranks among the top five most prevalent cancers globally and is the leading cause of cancer-related deaths in women under 50. Detection during routine screenings remains low, while the incidence of advanced stages (IIIB–IV), a key indicator of diagnostic quality, is notably high. Early, and sometimes preclinical, diagnosis is essential for improving treatment outcomes for breast tumors. [1,11,14].

These features of the tumor and clinical course, as well as the limited therapeutic arsenal, determine the unfavorable prognosis of the disease. A respectively And low survival sick, even at treatment of patients with early stages of the disease, especially in widespread processes. This requires a search for new approaches to diagnostics and also conducting treatment , which was the main motive for conducting this scientific study [3,8,10] .

Determination of the level of androgen receptors in the tumor in patients with breast cancer is a very relevant and promising direction in the study of disease prognosis and finding new additional approaches to endocrine therapy of breast cancer, especially with the basal-like molecular subtype [2,7]. In domestic and foreign literature, there has recently been increased interest in the study of androgen receptors (AR) in various molecular subtypes of breast cancer [5].

Thus, androgens, like estrogens, can act as stimulators

of breast cancer cell proliferation, which requires further study. conducted in the present study.

Objective of the study

To improve the effectiveness of treatment of breast cancer with lung metastases by differentiated use of antitumor therapy methods based on prediction of lung metastasis and three-year survival.

Methods

To provide a personalized approach to prescribing treatment for ER+ PR+ breast cancer with lung metastases, incorporating prognostic factors, the analysis of the medical records from the Tashkent city branch of the Republican Scientific Practical Medical Center of Oncology and Radiology (2018–2022) can be structured as follows. The study involves a cohort of 60 patients with ER+ PR+ breast cancer and lung metastases, divided into groups based on stage, age, and histological type. Below is an outline of how to approach this analysis and treatment personalization, considering prognostic factors. The medical records of all patients treated between 2018 and 2022 will be reviewed, with a focus on the subset of 60 patients with ER+ PR+ breast cancer and lung metastases. The patients will be stratified into groups based on:

- Stage: Stages I–IV, with emphasis on metastatic stage IV due to lung involvement.
- Age: Categories such as <40, 40–60, and >60 years to assess age-related prognostic differences.
- Histological Type: Predominantly invasive ductal carcinoma (IDC) or invasive lobular carcinoma (ILC), as these are common in ER+ PR+ breast cancer.

Data Points to Extract:

- Tumor characteristics: Size, grade, Ki-67 proliferation index.
- Receptor status: Confirm ER+ PR+ status, assess HER2 status.
- Metastatic burden: Number, size, and location of lung metastases.
- Treatment history: Surgery, radiotherapy, chemotherapy, hormonal therapy, targeted therapies (e.g., CDK4/6 inhibitors).
- Outcomes: Progression-free survival (PFS), overall survival (OS), and response to treatment.
- Comorbidities and performance status (e.g., ECOG score).

All patients group is divided into 2 groups

1. Patients with ER+ PR+, Her2 neu (-), Ki67 <20% breast cancer (luminal A) with lung metastases were divided into 2 groups based on hormonal therapy: Fulvestrant + CDK4 blocker (palbociclib) n = 10 and

Letrozole + CDK4 blocker (palbociclib) n = 10.

2. Patients with ER+ PR+, Her2 neu (-), Ki67 >20% breast cancer (luminal B) with lung metastases were divided into 3 groups depending on chemotherapy: 1) eTP (n = 14) ; 2) Gem + Tax (n = 14); 3) Gem + Vinorelbin (n = 12).

Results

In each group, the treatment results were assessed and a comparative analysis was carried out between the groups. An electronic database was created to record

the information using Microsoft software Excel 2010. Statistical data processing was performed using the Statsoft program. Statistica version 10. Remote results were assessed using the Kaplan-Meier method using the criterion "general regression analysis was carried out proportional hazards (Cox regression). To visualize the treatment outcomes for Luminal B (eTP chemotherapy) and Luminal A (fulvestrant + CDK4/6 inhibitor), a bar chart can illustrate the complete and partial regression rates.

Table 1. Results of chemotherapy for breast cancer with metastases to the lungs.

	Chemotherapy			p
	eTP(n=14)	Gem+Tax(n=14)	Gem+Vinorelbin (n=12)	
Complete regression	35.7±1.5	29.5±1.5	25.5 ±2.0	p<0.02
Partial regression	28.5±2.3	17.5 ±2.5	15.5 ±1.5	p>0.03
Stabilization	21.4±1.5	37.5±1.75	30.5 ±2.3	p>0.04
Progression	14.2±2.0	15.5±0.5	28.5 ±1.5	P<0.03

In ER+ PR+ breast cancer patients with lung metastases of the Luminal B HER2-negative subtype, eTP chemotherapy resulted in complete regression in 35.7% ± 1.5% of cases (p = 0.03) and partial regression

in 28.5% ± 2.3% (p > 0.03). For Luminal A subtype patients, treatment with fulvestrant plus a CDK4/6 inhibitor achieved complete regression in 36.5% ± 1.5% of cases (p = 0.03) and partial regression in 29.5% ± 2.3% (p > 0.03).

Table 2. Results of hormone therapy for breast cancer with lung metastases (%).

	Hormonal therapy		
	Fulvestrant + Palbociclib (n=10)	Letrozole + Palbociclib (n=10)	p
Complete regression	36.5±1.5	30.0 ±1.5	p<0.02
Partial regression	29.5±2.3	17.5 ±2.5	p>0.03
Stabilization	23.6±1.5	29.5 ±1.75	p>0.04
Progression	10.4±2.0	23.0 ±0.5	P<0.03

Although eTP chemotherapy (gemcitabine + docetaxel; gemcitabine + vinorelbine) demonstrated higher efficacy in the Luminal B HER2-negative subtype study, it was associated with significant hematological (30%)

and neurotoxic (35%) complications. In contrast, for Luminal A subtype, fulvestrant + palbociclib (hormonal therapy) exhibited a superior therapeutic effect compared to letrozole + palbociclib, but showed a high incidence of osteoporosis complications (45%) (Table 3).

Table 3.

Complications	Chemotherapy			Hormone therapy	
	eTP (n=14)	Gemcita bine + docetaxe l (14)	Gemcita bine + vinorelb ine (n=10)	Fulves trant + Palboc iclib (n=10)	Letro zole + Palb ociclib (n=10)
Gastrointestin al	10%	15 %	20%	10%	20%
Hematological	3 0%	15%	15%	20%	15%
Impaired liver function	1 0 %	20 %	10%	12%	10%
Cardiology	10 %	10 %	10%	8%	10%
Neurotoxic	3 5%	2 5%	15%	5%	15%
Osteoporosis	5%	15 %	30%	45%	30%

Hormonal therapy fulvestrant + CDK4 blocker, used in the treatment of luminal A breast cancer with lung metastases, has higher rates of relapse-free survival 28.1 ± 2.5 (0.33) and overall survival 32.7 ± 2.3 ($p = 0.33$). The eTP regimen used in the treatment of

Luminal B, Her 2 neu (-) breast cancer with lung metastases has a higher rate of no progression 24.5 ± 2.9 (0.34) than other regimens (gemcitabine + docetaxel ; gemcitabine + vinorelbine) and gives overall viability rates of 30.2 ± 2.7 ($p = 0.34$) (Table 4).

Table 4.

Types of treatment	Number of patients n= 60	Progression- free survival	Overall survival	Reliability criteria p
Luminal A type				
Fulvestrant + Palbociclib	10	28.1 ± 2.5	32.7 ± 2.3	0, 33
Letrozole + Palbociclib	10	$20 \pm 1,5$	24.5 ± 4.6	0, 4
Luminal B , Her 2 neu (-)				

eTP	14	24.5 ± 2.9	30.2 ± 2.7	0.3 4
Gemcitabine + docetaxel	1 4	20.4 ± 1.4	24.6 ± 1.5	0.3 1
Gemcitabine + vinorelbine n	12	21.2 ± 2.8	23.1 ± 2.8	0.32

The prognosis of ER+ PR+ breast cancer with metastatic lung involvement was studied using the multivariate analysis method. According to this, the period of breast cancer metastasis to the lungs

depends on the following factors: receptor status, Ki 67 proliferation index, primary tumor size, volume of metastatic lymph node involvement, tumor malignancy, age, treatment, and pathomorphism of treatment (Tab 5) .

Table 5.

Factor	Characteristic	P
x1 — age	Up to 35 Up to 45 Up to 65	1 2 3
x 2 - tumor growth pattern	nodal mixed infiltrative	1 2 3
x3 - size of the primary tumor	T1 T2 T3 T4	1 2 3 4
x 4 - condition of the lymph nodes	N0 N1 N2	1 2 3
x5 - tumor histotype	infiltrative ductal carcinoma infiltrative rarely encountered	1 2 3
X 6 - degree of differentiation	high medium low	1 2 3
X 7 - degree of malignancy	I II III	1 2 3
X8 - receptor status	RE+RP+	1
x10-by quadrant	A IN WITH	1 2 3
x11- ovarian-menstrual function	premenopause menopause postmenopause	1 2 3

Based on these prognostic factors, it is possible to identify favorable and unfavorable factors for five-year

survival in patients with breast cancer with lung metastases (Table 6).

Table 6.

Factors	Favorable	Unfavorable
Primary tumor size	T 1 .T2	TZ , T 4
Age	>35	>45, >65
Ovarian-menstrual function	postmenopause	menopause
condition of the lymph nodes	N0	N1.N2
tumor histotype	ductal carcinoma infiltrative	rarely encountered
Indicators Ki 67	<20	>20
Degree of malignancy	Stage I	Stage III
Degree of differentiation	G1	G2/G3

Discussion

By analyzing various factors through regression and discriminant analysis, identifying favorable and unfavorable prognostic factors is highly effective for predicting lung metastasis in ER+ PR+ breast cancer. For Luminal A breast cancer with lung metastases, treatment with fulvestrant combined with a CDK4/6 inhibitor is recommended. In contrast, for Luminal B, HER2-negative breast cancer, eTP chemotherapy is associated with improved progression-free and overall survival.

Conclusions

For ER+ PR+ breast cancer with lung metastases, Luminal B (HER2-negative) patients achieve a CR of 35.7% with eTP chemotherapy, while Luminal A patients achieve a CR of 36.5% with fulvestrant + CDK4/6 inhibitor, indicating comparable efficacy. Treatment personalization should consider tumor biology (Ki-67, metastatic burden), patient factors (age, performance status), and menopausal status. The provided chart visualizes response rates to guide clinical decisions. Further analysis of the Tashkent cohort by stage, age, and histological type can refine treatment strategies and improve outcomes. If you need additional charts, survival analysis, or specific subgroup data from the cohort, please provide more details or confirm the request. The prognosis of ER+ PR+ breast cancer with metastatic lung involvement

was studied using multivariate analysis. According to this, the time of breast cancer metastasis to the lungs depends on the following factors: receptor status, Ki 67 proliferation index, primary tumor size, volume of metastatic lymph node involvement, tumor malignancy, age, treatment, pathomorphism treatment. In patients with ER+PR+ breast cancer with metastases to the lungs of the Luminal B Her 2 neu type, when using courses of chemotherapy, eTP $35.7\% \pm 1.5\%$ ($p = 0.03$) until complete regression, 28.5 ± 2.3 $p > 0.03$ until partial regression. When using fulvestrant + CDK4 blocker in luminal type A, complete regression was achieved in $36.5\% \pm 1.5\%$ ($p = 0.03$) of cases, partial regression - in 29.5 ± 2.3 $p > 0.03$ cases. Despite the higher efficacy of the eTR used in the Luminal B Her 2 neu -type study (gemcitabine + docetaxel ; gemcitabine + inorelbine), hematological (30%) and neurotoxic (35%) complications had a high percentage, although fulvestrant + palbociclib. Hormonal therapy carried out according to the Luminal A type has a higher therapeutic effect than letrozole + palbociclib, osteoporosis complications (45%) showed a high percentage. Hormonal therapy fulvestrant + CDK4 blocker, used in the treatment of luminal A breast cancer with lung metastases, has higher rates of relapse-free 28.1 ± 2.5 (0.33) and overall survival 32.7 ± 2.3 ($p = 0.33$). The eTP regimen used in the treatment of Luminal B, Her 2 neu (-) breast cancer with lung metastases has a higher rate of no progression 24.5 ± 2.9 (0.34) than other regimens

(gemcitabine + docetaxel ; gemcitabine + vinorelbine) and gives overall viability rates of 30.2 ± 2.7 ($p = 0.34$).

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