APPLICATION OF LAPATINIB IN PATIENTS WITH HER-2 POSITIVE METASTATIC BREAST CANCER

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Relevance. Initially, HER2-positive breast cancer was one of the most aggressive types of this disease, which was characterized by a very rapid tumor growth rate, a high risk of disease relapse and the appearance of distant metastases. In developed countries, in the structure of cancer incidence in women, breast cancer (BC) ranks 1st or 2nd (20–25% of all cancer cases). More than half of patients with breast cancer develop distant metastases at one stage or another of the disease. Metastatic breast cancer (mBC) is an incurable disease, but modern treatment approaches allow achieving clinically significant results. The identification of more and more new molecular genetic and immunohistochemical markers and their correlations makes it possible to individualize treatment tactics for patients [1]. The most significant factors for poor prognosis in mBC include overexpression of HER2, a transmembrane receptor with tyrosine kinase activity, which is the result of amplification of the HER2 gene on chromosome 17 [2,3,11]. Studies have shown that the HER2-positive subtype is more common among young women with advanced stages of the disease, is characterized by high aggression and rapid dissemination of the tumor process, and does not depend on the size of the tumor. Even with minimal carcinoma sizes and in the absence of involvement of regional lymph nodes, HER2 overexpression is associated with an unfavorable course of the disease [3, 4]. Today, determination of HER2 status in breast cancer is mandatory for all stages of the disease; it is necessary to assess the prognosis and develop an optimal treatment algorithm. Determination of HER2 status in a tumor is standardized and is performed on paraffin blocks of the tumor using immunohistochemical analysis and, in case of questionable analysis results (HER2-2+), is supplemented by determining gene amplification using in hybridization situ (ISH) [5–7]. Anti-HER2 therapy is currently the standard approach to the treatment of breast cancer patients with HER2 overexpression or HER2 gene amplification and usually complements chemotherapy or hormonal therapy [14,15]. Lapatinib is an antibody-drug conjugate that delivers the latter directly to HER2-positive cancer cells, thereby limiting damage to healthy tissue [8,9,12]. The use of Lapatinib can increase efficacy and achieve tumor control in young patients with HER-2 positive mBC .

Purpose of the study. Analysis of the immediate effectiveness of Laratinib in patients suffering from HER-2 positive mBC .

Material and methods. The study included patients with metastatic breast cancer HER-2 positive status - 15 patients with mBC , aged from 32 to 65 years, average age 43 years, who had progression after adjuvant chemotherapy or hormone therapy with Lapatinib, or progression on the 1st line chemotherapy and Lapatinib. The drug was prescribed at a dose of 3.6 mg/kg once every 3 weeks. Previous treatment – 6 (40%) patients progressed with trastuzumab in the adjuvant, 5 (33.3%) with hormone therapy and capacitabin, 4 (26.7%) with capesitabin and Lapatinib. In 5 patients (33.3%) more than 3 organs and systems were involved in the process. In patients with metastatic lesions of 1 organ in 6 (40%), combined lesions of the lungs and brain in 3 (20%). Therapy was continued until maximum effect or progression was achieved. 21 days after completion of the 3rd and 6th courses of PCT, ultrasound of the mammary glands, regional areas, MSCT of the chest and abdominal cavity with contrast was performed, determining the volume of the breast tumor and the size of the lymph nodes, metastatic foci in the lungs and liver. The rate of immediate antitumor response was assessed according to RECIST criteria. The selection of the main characteristics and statistical criteria for their comparison was carried out after studying the distribution of the characteristic and comparing it with the Gaussian distribution using the Kolmogorov-Smirnov criterion. For numerical characteristics with a distribution corresponding to the Gaussian distribution, the average values of numerical characteristics and the standard error of the mean were calculated. The significance of differences P was calculated by discriminant analysis. If the number of groups was more than two, P was calculated taking into account multiple comparisons (according to the Scheffe test). For traits with a distribution significantly different from normal, the median, quartiles were calculated, and nonparametric methods for comparing unrelated traits were used (Kruskal-Wallis Anova & Mediantest when the number of groups being compared is more than two and Mann-Whitney when comparing two groups). When comparing frequencies, contingency tables of characteristics were constructed. To calculate P, Fisher's exact test (for small group sizes) and the nonparametric ci-2 test were used.

Results. During treatment, the overall response was 60.0% (13 patients), of which 1 (6.6%) patient had complete remission, partial remission in 5 (33.3%), stabilization of the process in 6 patients (40%) , process progression in 1 patient (665%). The median relapse-free survival was not reached, given the short follow-up period. Overall disease-free survival was 51.4%. The median overall survival was 9 months. Overall 1-year survival rate was 61.3% ($p < 0.001$). When studying the toxicity of chemotherapy, we analyzed 15 chemotherapy courses. According to publications, the most common serious side effects include asthenia, thrombocytopenia, vomiting,

and abdominal pain. Of the non-hematological complications in our group of patients, gastrointestinal complications predominated (72%). Of these (gastrointestinal complications), nausea was most often observed - in 26.3%, abdominal pain - 26.3%. In general, it should be noted that the drug is well tolerated, despite the listed possible side effects, attention should be paid to grade 1–2 asthenia – 73.7%. Side effects were mostly mild, and when they appeared in the 3rd degree, they were more adequately amenable to drug correction. Having our own experience with the use of the drug Lapatinib, I would like to demonstrate the most impressive result of using the drug in the first line of treatment of metastatic HER2-positive breast cancer with progression during adjuvant therapy with the drug Lapatinib.

Conclusions. Our analysis of the use of the drug Lapatinib showed that the drug is well tolerated and highly effective in young patients with HER-2 positive metastatic breast cancer. The data obtained on relapse-free and overall survival confirm the opinion of many authors about the effectiveness of the drug Lapatinib in the group of patients previously treated with capacitabin and lapatinib, and the duration of the studied parameters corresponded to the literature data.

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