

NEW APPROACHES TO BREAST CANCER TREATMENT

¹Khomidova Tursunoy Ergashboy kizi, ²Israiljonov S.

¹Independent researcher of Fergana State University, Faculty of Natural Sciences, Department of Zoology and General Biology

²Candidate of biological sciences, associate professor

<https://doi.org/10.5281/zenodo.8283472>

Abstract. *Over the past years, there has been significant progress in many aspects of the treatment of breast cancer (BC). The genomic atlas, outlining the heterogeneity of breast cancer, indicates that genomic studies will help in treatment planning. More and more data are accumulating on the feasibility of complete axillary dissection, the optimal duration of therapies.*

Keywords: *breast cancer, surgery, radiation therapy, biological subtypes, systemic treatment.*

INTRODUCTION

Surgery remains the main treatment for breast cancer. The classical international TNM staging system is the basis for the planning of primary treatment: surgical for surgical tumors and neoadjuvant systemic therapy for non-operative tumors, as well as for patients with surgical tumor (T2N1M0) in order to perform organ-preserving surgery instead of radical mastectomy.

MATERIALS AND METHODS

Thanks to the widespread introduction of mammography screening and the success of radiotherapy in many countries, organ-sparing treatment of breast cancer (BC) is increasing or even predominating. When planning organ-preserving operations, the most important issue is an accurate assessment of contraindications to their implementation. Conference experts St. Gallen determined relative contraindications to organ-sparing operations: age under 35 years (30% of those who voted), presence of diffuse microcalcification on mammograms (70% of those who voted), multicentricity of tumor foci according to MRI (76.9 % of those who voted), its location to the nipple-areolar complex (42.6% of those who voted), mutation of the BRCA and/or BRCA2 genes (51-54.3% of those who voted). When performing a sectoral or segmental resection, a thorough pathomorphological examination of the surgical preparation may reveal signs requiring a wider excision of the wound edges and performing a mastectomy with “positive” edges, including DCIS [1]. The presence of an extensive intraductal component (EIC), extensive invasion of the lymphatic and blood vessels, only 34% of experts refer to relative contraindications for performing organ-preserving operations. Lobular invasive cancer, BC according to the gene-expression profile 93.8% of experts St. Gallen does not refer to contraindications for performing organ-preserving operations (if there are no contraindications to subsequent radiation therapy).

RESULTS AND DISCUSSION

Manipulations in the axillary region are considered in the general context of organ-preserving treatment. Limited removal of one to three lymphoids using a signal (sentinel) is considered to be indicated in all patients with clinically negative (cN0) lymphocytes [2]. If one or two sentinel lymphoid cells contain tumor micrometastases, St. Gallen considered it possible not to perform a complete axillary dissection [3]. The vast majority of experts (95.1%) consider it necessary to perform a complete axillary dissection in the presence of 3 and 6 more “positive” signal lymphatic words.

The next component of local treatment - postoperative radiation therapy - is considered mandatory after organ-preserving operations, however, in old age and in the presence of severe concomitant salivation, radiation therapy should be abandoned (opinion of 68% of experts). Methods of accelerated (hypofractional) radiation therapy (40 Gy sa 15 fractions) are supported, but so far there is no general agreement among experts in relation to intraoperative radiation therapy for T1-2N0 tumors [4]. Radiation therapy is considered from the point of view of the Oxford meta-analysis of randomized trials, which included about 10 thousand patients. It follows from the Oxford speaker that almost all patients, even those with the earliest stages of BC (T1-2N0M0), require radiotherapy after organ-sparing surgery, which reduces the absolute 10-year risk of recurrence of SA6 disease from 35% to 19.3% (by 15.7%) and 15-year risk of death from BC from 20.5% to 17.2%. In women with regional metastases, radiotherapy reduced the 10-year risk of recurrence from 63.7% to 42.5% and reduced the 15-year absolute risk of death from BC from 51.3% to 42.8% ($p = 0.001$). Partial (partial) leprosy of the mammary gland after organ-preserving surgery can be performed in the absence of the above risk factors for recurrence, and also as a replacement (boost) therapy on the tumor bed [5]. Radiation therapy after mastectomy should be the standard for patients with metastatic lesions of four and more axillary tracts ($pN+\geq 4$). In patients with lesser axillary lymphoid involvement ($pN+1-3$), postoperative radiotherapy is recommended in the presence of the aforementioned pathological risk factors, in patients younger than 40 years of age, and in patients with positive ($pN+$) sentinel lymph nodes who have not undergone axillary dissection. According to expert radiologists at St. Gallen, radiotherapy after mastectomy is also recommended in the presence of morphological risk factors for recurrence (opyx size ≥ 5 cm and positive margins of the surgical preparation) [67.3% and 82.2% — experts].

Systemic adjuvant treatment

Systemic treatment planning is mainly based on the identification of 6 biological subtypes of BC. For practical purposes, immunohistochemical subtyping is allowed, taking into account the expression of ER, PR, HER2 and Ki67. If there are no conditions for determining Ki67, it is allowed to determine the amount of expression of progesterone receptors (PgR), but not the degree of malignancy (G) to distinguish luminal A from luminal B BC (as was also allowed in the St. Gallen- classification). The vote did not determine the lower expression threshold for Ki 67 to identify these subtypes: $\geq 14\%$ or $\geq 20\%$ [6].

BC subtypes

To determine the biological subtype of BC, the use of multigenic expression profiles (such as PAM50) has been ideal, but clinicomorphological subtyping (HX) (supported by St. Gallen) is still considered quite acceptable [3]. According to experts (St. Gallen), the choice of a specific chemotherapy regimen is hardly determined only by the molecular genetic subtype (intrinsic subtype). Determination of multigenic signatures (for example, Oncotype DX - risk scores) is especially important in luminal B (Her2 - negative) BC, as well as in patients with "positive lymphocytes" ($pN+$) (ER[+] Her2 -) to predict the further course of SA6 treatment, and, most importantly, to predict sensitivity to adjuvant chemotherapy.

Endocrine Therapy

The standard endocrine therapy for premenopausal age remains tamoxifen, with the possible addition of ovarian function suppression in young women (<40 years). Premenopausal women with a contraindication to the use of tamoxifen may be prescribed aromatase inhibitors along with suppression of ovarian function (OFS) [4].

Endocrine therapy in postmenopausal women

Some women may be treated with tamoxifen. Aromatase inhibitors may be started initially (up-front), especially in women at high risk of relapse, or sequentially (after 2 years of tamoxifen therapy). Aromatase inhibitors may also begin after 5 years of tamoxifen treatment, especially in patients with lymphoid metastases (pN+) [2].

Tamoxifen, judging by the results of the ATLAS program, can be started for a period of more than 5 years (up to 10 years), preferably in patients with contraindications or poor tolerance to aromatase inhibitors [5].

Chemotherapy

To the factors arguing the appointment of adjuvant chemotherapy, the experts of St. Gallen include the following features:

- Histological grade 3 (G3) tumor quality (84.4% of experts).
- Low hormonal receptor status (75.5% of experts).
- Positive HER2 status (91.8% of experts).
- Triple negative tumors (98% of experts).
- High (>14%) Ki67 value (75.5% of experts).
- High value of the risk scale (>25) of the 21-gene signature (Oncotype DX-RS) (93.9% of experts).
- Presence of more than 3x positive (metastatic) lymph nodes and young (<35 years) age of the patient (93.9% of experts).

Preferred specific chemotherapy regimens for any BC phenotype have not been defined, but wishes have been made for the “connection” of taxanes and anthracyclines in HER+ positive and basal subnoma BC.

Anti-HER2 Therapy

The minimum tumor size requiring the appointment of trastuzumab was defined as category pT1a (5 mm) [71.5% of St. Gallen]. In receptor-positive (ER+/PR+) opyxols, when there are contraindications to chemotherapy, it is necessary to start trastuzumab together with endocrine therapy. In receptor-negative tumors (ER-), in the presence of contraindications to chemotherapy, it is possible to prescribe one trastuzumab (targeted monotherapy). The international HERA study showed that the preferred duration of adjuvant therapy with trastuzumab is 12 months [6].

CONCLUSION. Monitoring of patients with early BC (after primary treatment)

- There is no need for regular follow-up by surgeons/oncologists of all patients after treatment (with the exception of long-term endocrine therapy).
- Regular monitoring by specially trained nurses (supported by 77.3% of experts), as well as by telephone survey (only 22.9% of experts) is considered acceptable.
- A patient who has completed treatment should undergo regular mammography. Other routine imaging methods (CT, MRI, PET) during observation are not clear.

These, in brief, are the new approaches to BC therapy that are being proposed and will be tested in future studies.

REFERENCES

1. V.F. Semiglazov, V.V. Semiglazov, and A.E. Neoadjuvant and adjuvant treatment of breast cancer. M. Medinform agency. - 2018. - 288 p.

2. Burstein HJ. Triple-negative breast cancer: Is there an optimal adjuvant treatment? // *The Breast*.— 2013.-Vol. 22 (Supp 1). — p. S16 (Abstr. SP9.02).
3. Cheang MCU, Chia SK, Voduc D et al. Ki67 Index, HER2 Status, and Prognosis of Patients With Luminal B Breast Cancer // *J Natl Cancer Inst.* - 2019. - Vol. 101. - p. 736-750.
4. Львов, Д. К., Щелканов, М. Ю., Бовин, Н. В., Малышев, Н. А., Чучалин, А. Г., Колобухина, Л. В., ... & Маслов, А. И. (2012). Корреляция между рецепторной специфичностью штаммов пандемического вируса гриппа А (H1N1) pdm09, изолированных в 2009-2011 гг., структурой рецепторсвязывающего сайта и вероятностью развития летальной первичной вирусной пневмонии. *Вопросы вирусологии*, 57(1), 14-20.
5. Sobirzhonovna, B. N., Bosimovich, M. B., & Asadovna, K. G. (2022). Comparative Evaluation of MMP and Cystatin C in Chronic Nephritic Syndrome in Children. *Eurasian Medical Research Periodical*, 8, 122-124.
6. Базарова, Н. С., Абдурахманова, Р. А., & Турсунова, Г. Р. (2021). Связь матриксных металлопротеиназ-9 и цистатина с при хроническом гломерулонефрите у детей. *Евразийский журнал академических исследований*, 1(9), 740-742.
7. Sobirjonovna, B. N., & Khudoyberdievich, Z. S. (2022). Comprehensive assessment of various forms of chronic chronic nephritic syndrome in children.
8. Sobirjonovna, B. N., & Azizxonovna, N. M. (2023). CHAKANDA O'SIMLIGIGA ZAMONAVIY QARASHLAR. *journal of innovations in scientific and educational research*, 6(2), 209-211.
9. Sobirjonovna, B. N., & Khudoyberdievich, Z. S. (2022). Comprehensive assessment of various forms of chronic chronic nephritic syndrome in children.
10. Otaqo'ziyevna, T. M., & Abdualiyevna, A. F. (2022). THE ROLE AND ROLE OF VIRTUAL TECHNOLOGIES IN SOLVING INTERDISCIPLINARY APPLIED ISSUES ON NEWTON'S LAWS AT SCHOOL. *Galaxy International Interdisciplinary Research Journal*, 10(12), 118-121.
11. Otaqo'Ziyevna, T. M., & Xonzodabegim, A. (2022). YORUG'LIKNING TARQALISHI, QAYTISHI VA SINISHI MAVZUSINI ZAMONAVIY PEDAGOGIK TEXNALOGIYALARI ASOSIDA TASHKIL ETISH USULLARI. *Ta'lim fidoyilari*, 22(7), 452-457.
12. Ismatullayev, N. A., Homidjonov, A. O. U., & Tohirova, M. I. Q. (2021). Creating A New Range Of Boots For Young Children. *The American Journal of Engineering and Technology*, 3(06), 106-112.
13. Urazaliyeva, I., Nematov, A., & Tolipova, G. (2023). ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ COVID-19 И ВИДЫ МЕДИКО-СОЦИАЛЬНОЙ ПОМОЩИ ОКАЗЫВАЕМОЙ БОЛЬНЫМ.
14. Толипова, Г. К., & Маматмусаева, Ф. Ш. (2022). МИКРОСКОПИЧЕСКИЙ СОСТАВ ЖЕЛЧИ У ДЕТЕЙ ВИРУСНЫХ ГЕПАТИТАХ «А», «В» и «С». *Евразийский журнал академических исследований*, 2(11), 172-179.
15. Mamatkulov, B., Tolipova, G., Adilova, Z., & Nematov, A. (2023). ПРОБЛЕМЫ ИММУНОПРОФИЛАКТИКИ: ФАКТОРЫ ВЛИЯНИЕ НА ФОРМИРОВАНИЕ ОТНОШЕНИЯ К ИММУНОПРОФИЛАКТИКЕ.