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Voxidova Zebo Tolibovna
Stajor-assistant, candidate of medical sciences
Department of Operative Surgery and Topographic Anatomy Samarkand State Medical University

RESEARCH STATUS OF SYSTEMIC ADJUVANT THERAPY FOR EARLY BREAST CANCER

Resume: In recent years the level of lung cancer that has given way to breast cancer as the leading cause of cancer deaths worldwide. Treatment can be effective in the early stages of breast cancer, and patients receiving conventional therapy typically have a longer life expectancy. Further investigation of the early stages of the disease could lead to an expanded range of therapeutic alternatives that could improve prognosis and increase survival of breast cancer patients.
Key words: early breast cancer, adjuvant systemic therapy, hormone receptor-positive breast cancer, HER2 breast cancer.

Research Status of Systemic Adjuvant Therapy for Early Breast Cancer

Abstract

Lung cancer has been surpassed by breast cancer as the primary cause of cancer-related fatalities worldwide. Treatment can be effective for early-stage breast cancers, and patients who receive traditional therapy typically have higher life periods. Over the years, there has been a significant shift in the treatment of breast cancer from radiation and surgery to systemic and local adjuvant medications. Therapeutic treatment is available for localized breast cancers, however distant recurrences might induce morbid rate. Because adjuvant systemic therapy is effective for both local and distant recurrences, it has attracted a lot of interest. Over the past three decades, the prognosis for early-stage breast cancer has improved dramatically with a decrease in mortality rates, largely due to the widespread use of adjuvant therapy. Because postoperative adjuvant therapy can increase the disease's cure rate, it is currently included in the comprehensive treatment plan for breast cancer. Further investigation into the early stages of the disease may lead to an expansion in the range of therapeutic alternatives that can improve the prognosis and survival advantages for patients with breast cancer.

Keywords: early breast cancer, adjuvant systemic therapy, hormone receptor-positive breast cancer, HER2 breast cancer

Introduction

With a high annual incidence of 11.7%, breast cancer has surpassed lung cancer to become the most common cancer as of 2020. Nevertheless, it still ranks fifth globally in terms of cancer-related mortality. 1. At the time of clinical presentation, 3 percent of patients with breast cancer have a tumor that has spread regionally, 7% have metastasized, and 61% have a localized tumor. 2 Because of a better understanding of the clinical and pathologic features of the illness, advances in breast cancer treatment have led to a de-escalation of radiation and/or radical mastectomy. Progression has resulted from an increase in the use of multimodal therapy, which consists of chemotherapy, targeted therapy, endocrine therapy, and immunotherapy.

Numerous clinical trials have shown that adjuvant systemic chemotherapy, endocrine therapy, and anti-HER2 therapy can enhance survival and decrease recurrence in individuals with early-stage breast cancer. 2. Those with breast cancer who are able to receive adequate therapy now have a 90% probability of making a full recovery because to increased therapeutic options. Adjuvant systemic therapy optimization has received a lot of interest since it has increased the survival rates of patients with early-stage breast cancer. 5. In the current context, women with early-stage breast cancer can benefit from systemic treatment lasting more than 10 years, given a decreased chance of harm. 4. This review covers the most current developments in adjuvant therapy for early breast cancer, with special emphasis on chemotherapy, endocrine therapy, targeted therapy, bone-modifying medication therapy, and adjuvant intensive therapy following neoadjuvant therapy. Table 1 provides a review of the clinical results of several research studies on various adjuvant therapy in individuals with early-stage breast cancer.

Methods of research

Adjuvant chemotherapy

Chemotherapy is an essential part of treating breast cancer all the way through. Chemotherapy has been shown to improve prognosis and enhance survival in early-stage breast cancer patients. However, issues with medicine resistance and side effects caused by chemotherapy need to be addressed.6. It is often recommended that women with high-risk node-negative or resected node-positive breast cancer have an adjuvant chemotherapy regimen that includes anthracene.

Consequently, in order to prevent cardiotoxicities, non-anthracycline-containing regimens are becoming increasingly and more common for patients with early-stage breast cancer. 8

Triple-Negative Breast Cancer

Triple-negative breast cancers (TNBCs), which are frequently characterized by heterogeneity, aggressiveness, and a poor prognosis, have traditionally been treated exclusively with chemotherapy.14, 15, In the neoadjuvant phase, chemotherapy is still the main therapeutic option for TNBC, despite the effectiveness of programmed cell death 1 (PD1), programmed cell death ligand 1 (PD-L1), and poly (ADP-ribose) polymerase (PARP) inhibitors. 15.

There are currently no published studies in early TNBC adjuvant settings, and there is ongoing exploration of the best combination and management of side effects when employing combination medicines.

Hormone Receptor-Positive Breast Cancer

In Western countries, 70 percent of cases of breast cancer are hormone receptor (HR)-positive (i.e., ER- and/or PR-positive) and human epidermal growth factor receptor 2 (HER2)-negative breast cancer. Merely 15% of women with breast cancer who get adjuvant endocrine therapy experience a recurrence within a decade or less. For these patients, adjuvant chemotherapy lowers the chance of a breast cancer recurrence. As a result, the majority of patients were recommended to have adjuvant chemotherapy by the National Institutes of Health, which reduced the death rate among those with breast cancer. Most patients undergo adjuvant chemotherapy needlessly, and 85% of women can avoid treatment because to the low relative risk of recurrence and limited effectiveness of chemotherapy. As a result, a crucial topic of current research is developing a screening and identification system for breast cancer patients who may benefit from chemotherapy. The clinicopathologic features of patients and the outcomes of multi-gene testing serve as the primary foundation for the risk assessment of postoperative recurrence. More auxiliary tools for early breast cancer diagnosis, prediction, and treatment have been made available with the introduction of multi-gene testing. Decisions for adjuvant chemotherapy, radiation therapy, and endocrine therapy can be made based on the evaluation of individual patient prognoses and the prediction of therapeutic effects by the detection of specific gene expression. Currently, the majority of multi-gene assays that are advised by both international and local consensus include Breast Cancer, Oncotype Dx® (21 genes), MammaPrint® (70 genes), and RecurIndex® (28 genes).

The optimization of current chemotherapy regimens for the treatment of HR-positive breast cancer is a constant goal. Research is needed to determine whether

dose-dense chemotherapy is beneficial in early-stage HR-positive breast cancer cases. Dose-dense chemotherapy is currently recommended as a standard postoperative adjuvant chemotherapy for high-risk patients in both domestic and international recommendations. Notably, the dose-dense regimen somewhat upsets the equilibrium between safety and efficacy, placing additional demands on medical professionals.

HER2-Positive Breast Cancer

A rising number of research, concerned about the high toxicity and side effects of anthracyclines, have started to investigate if avoiding them can improve the prognosis of patients with breast cancer. Patients with early-stage, low-risk HER2-positive breast cancer were the first to get this treatment. With tumor sizes of less than 1 cm and between 1.1 and 2.0 cm, the 2-year DFS rate was 100% and 98.1%, respectively, in axillary node-negative patients undergoing the TCH (docetaxel + cyclophosphamide + trastuzumab) regimen for HER2-positive early breast cancer patients.

This study validates the effectiveness of TCH regimen as adjuvant treatment for patients with HER2-positive breast cancer. In patients with node-negative, early HER2-positive breast cancer and tumors less than 3 cm, the single-arm APT research investigated the effectiveness and safety of adjuvant paclitaxel with TH. Propensity-score matching (PSM) revealed that patients who got TH with chemotherapy without paclitaxel had comparable invasive disease-free survival (IDFS) (96.5% vs. 92.9%) and overall survival (OS) (99.3% vs. 97.4%) to those who received paclitaxel and TH; however, the latter group saw a reduced incidence of adverse events. Chemotherapy "subtraction" based on maintaining efficacy has progressively begun to show benefits for lowering the impact of unpleasant effects on patients and enhancing quality of life.

Adjuvant Targeted Therapy

In particular, patients with HER2-positive breast cancer had a lower chance of recurrence when adjuvant targeted therapy that targets molecular pathways was administered. Twenty to thirty percent of tumors related to breast cancer overexpress or amplify HER2. Due to its extreme aggression and malignancy, this molecular subtype raises the risk of metastasis and mortality. When given in conjunction with chemotherapy in adjuvant circumstances, anti-HER-2 monoclonal antibody TH has been demonstrated to improve DFS (84%) and OS (92%) in patients with HER2-positive early breast cancer. Prior to the past 20 years, TH was the sole anti-HER2 medication on the market, but the field of HER2-targeted medications has undergone continuous change. New medications

that have considerably improved patient outcomes as a result of this include pertuzumab, lapatinib, trastuzumab emtansine (T-DM1), and trastuzumab deruxtecan (DS8201).

The results indicate that adjuvant targeted treatment, in the absence of chemotherapy, may be a viable substitute for the taxane-based trastuzumab regimen, without sacrificing clinically meaningful toxicities.

Results

Adjuvant chemotherapy has show effective treatment for early stage of breast cancer. Anthracyclines have been shown to be efficacious in numerous large cohort studies. Patients with early-stage breast cancer had better disease-free survival (DFS) and overall survival (OS) when taxane was added to an anthracycline-based treatment as an adjuvant.7. For the last thirty years, anthracycline-based regimens have been the mainstay of adjuvant chemotherapy; however, the National Comprehensive Cancer Network (NCCN) has connected these to long-term cardiotoxicity.

Triple-Negative Breast Cancer

The implementation of standardized chemotherapy regimens and the creation of appropriate strategies for the management of adverse responses are the main goals of adjuvant chemotherapy for early TNBC. In the BGIRG005 study, adjuvant therapy for early-stage triple-negative breast cancer was compared between AC-T (doxorubicin + cyclophosphamide followed by docetaxel) and TAC (docetaxel + doxorubicin + cyclophosphamide). The efficacy of DFS and OS did not differ considerably, however AC-T exhibited a notably greater level of hematological toxicity in comparison to the combination therapy. Adjuvant chemotherapy with AC-T may be chosen in high-risk TNBC patients because to its low tolerance and toxicity. Patients with early-stage, triple-negative breast cancer who finished standard adjuvant therapy were given capecitabine maintenance medication for a year as part of the SYSUCC-001 trial. The 5-year DFS with capecitabine (82.8%) was substantially better than the control group's (73.0%) after a median follow-up of 56.5 months. Consequently, the chance of recurrence may be decreased by selecting conventional therapy and then starting capecitabine medication for a year.

1 A meta-analysis of nine randomized clinical studies involving TNBC patients receiving combination capecitabine regimens as neoadjuvant and adjuvant chemotherapy revealed much better OS (HR =.63; 95% CI;.53–.77; P <.001) and DFS (HR =.75; 95% CI;.65–.86; P <.001). 15 Chemotherapy and immunotherapy have been linked to efficacious treatment for early-stage breast cancer and as a curative measure for breast cancer that has spread to other areas of the body.

Hormone Receptor-Positive Breast Cancer

The effectiveness of chemotherapy regimens without anthracene has recently been the subject of numerous trials, particularly for patients with HER2-negative breast cancer, where it was determined to be a feasible substitute.The ELEGANT Phase III research is the first open-label, randomized, prospective clinical trial that compares the safety profile of docetaxel and cyclophosphamide (TC) with that of epirubicin and cyclophosphamide (EC). Chemotherapy regimens for patients with node-negative, low-risk luminal breast cancer appear to be beneficial, as the study's first findings showed comparable efficacy outcomes for EC and TC at no discernible difference in survival. Dose-dense and standard chemotherapy regimens were evaluated for efficacy in a meta-analysis involving 37,298 participants from 26 clinical studies that were part of the EBCTCG. A dose-dense regimen incorporating taxanes, administered every two weeks, was found to be able to reduce both the rate of recurrence (24.0% vs. 28.3%) and the death rate from breast cancer (16.8% vs. 19.6%) when compared to the usual regimen (10 doses every three weeks). Treating patients with early-stage, high-risk breast cancer with dose-dense chemotherapy may reduce treatment duration and increase long-term survival benefits.

Adjuvant Targeted Therapy

According to the APHINITY research, in early HER2-positive breast cancer patients, adding pertuzumab to TH plus chemotherapy reduces the recurrence rate (7.1% vs 8.7%, P = 0.045) and lengthens the IDFS (94.1% vs 93.2%). Dual-targeted therapy is now part of the standard of care for patients with HER2-positive breast malignancies, according to this study. APHINITY research data was then updated and included an 8.4-year follow-up. The results revealed an OS hazard ratio (HR) of.83 (95% CI:.68–1.02; P =.078) and an 8-year OS rate of 92.7% vs. 92.0% for single-targeted therapy and dual-targeted therapy, respectively. With regard to the node-positive (N+) group, the updated IDFS HR was.77 (95% CI:.66–.91) and.72 (95% CI:.60–.87).

In the ATEMPT trial, 497 patients with stage I HER2-positive breast cancer were randomized to receive trastuzumab emtansine monotherapy or trastuzumab regimen for a year. According to the findings, a year of adjuvant trastuzumab emtansine was linked to a very good three-year iDFS. With a 3-year IDFS rate of 97.8% and a relapse-free survival (RFS) rate of 99.2%, the trastuzumab emtansine group saw fewer recurrent episodes.

Conclusion

Treating patients with early-stage, high-risk breast cancer with dose-dense chemotherapy may reduce treatment duration and increase long-term survival

benefits. Treatment options for patients with early-stage HER2-positive breast cancer who are receiving adjuvant therapy have expanded with the development of antibody drug conjugates. The development of HER2-targeted medications is a significant advancement in the treatment of breast cancer and allows physicians to create more effective, individualized regimens for their patients with HER2-positive disease.

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