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BREAST CANCER: AN OVERVIEW OF BREAST CANCER THERAPY

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ABSTRACT:

The health of women worldwide is gravely threatened by breast cancer, the most prevalent cancer diagnosed and the main cause of death for female patients. Multidisciplinary collaboration and consideration of tumor load and molecular makers are necessary for the treatment of breast cancer. The standard of care for early-stage breast cancer is still breast-conserving surgery combined with radiation therapy or mastectomy alone. The condition of lymph nodes, hormone receptors, and human epidermal growth factor receptor-2 determines whether adjuvant systemic therapy is administered. Treatments for metastatic breast cancer aim to preserve quality of life and increase survival. This review will present the current advances and controversies of surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, immunotherapy, gene therapy, and other innovative treatment strategies in early-stage and metastatic breast cancer.

Keywords: breast cancer, surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, immunotherapy, gene therapy

INTRODUCTION :

Breast cancer is the primary cause of cancer-related mortality and the most prevalent malignancy diagnosed in female patients. One According to the 2023 estimate, invasive breast cancer accounted for around 30% of all malignancies in women in the United States, with 300,590 new cases and 43,700 fatalities[1].Surgery, chemotherapy, radiotherapy (RT), endocrine therapy, targeted therapy, and immunotherapy are among the treatments for breast cancer. The treatment plans necessitate the collaboration of several subspecialties. The usual course of treatment for non-metastatic breast cancer is surgery. Additionally, preoperative systemic therapy based on chemotherapy can decrease the breast tumor's volume, allowing for breast conservation and lowering the necessity for axillary lymph node dissection (ALND). [2] Systemic treatment remains the preferred Option for metastatic breast cancer, and surgery is only used for palliative therapy in selected

metastatic patients[3]. The Advances in endocrine therapy, targeted therapy, and immunotherapy provide additional treatments for patients with metastatic And nonmetastatic breast cancer. Some innovative therapies are also being investigated, such as gene therapy, vaccines, Adoptive cell therapies, including T cell receptor therapy and chimeric antigen receptor T (CAR-T) therapy, and achieved Promising results. This review aims to summarize the current status and controversies of surgery, chemotherapy, RT, endocrine Therapy, targeted therapy, immunotherapy, gene therapy, and other innovative therapies in breast cancer, and provides better Management for oncologists[4]

SURGERY:

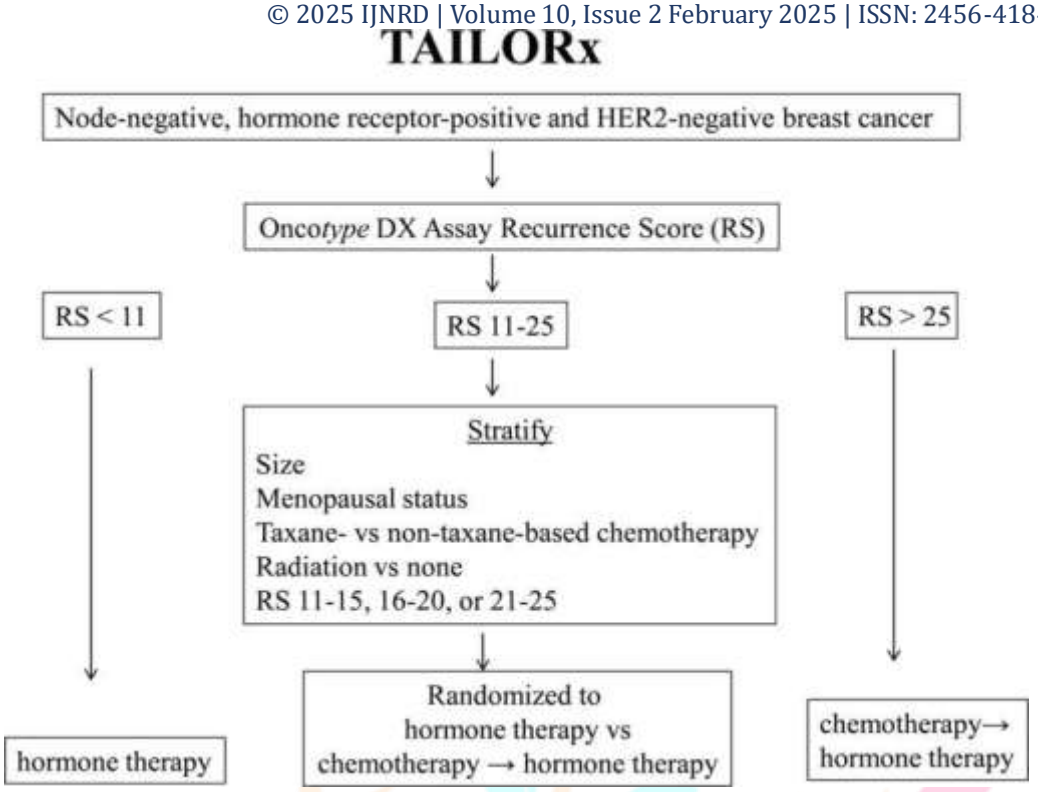
1. **Surgical Option: Breast-Conserving Surgery, or Lumpectomy:** This procedure removes just the tumor and a tiny margin of surrounding tissue. A mastectomy involves removing one or both breasts completely. Only the breast tissue is removed during a simple mastectomy. A radical mastectomy, which is rarely performed these days, involves removing the breast along with the underlying muscles and lymph nodes. More breast skin is preserved with a skin-and breast-sparing mastectomy, which improves the results of reconstruction [5]

2. **Lymph Node Surgery: Sentinel Lymph Node Biopsy (SLNB):** Determines whether lymph nodes have been affected by malignancy. If cancer is found, several lymph nodes are removed during axillary lymph node dissection (ALND)[6]

3. **Adjuvant Therapies (Treatments After Surgery):** Radiation therapy is used to kill any cancer cells that remain after a mastectomy or lumpectomy. Chemotherapy: Often used for aggressive or advanced tumors, this systemic treatment either kills or stops the proliferation of cancer cells. Hormone treatment. Blocking estrogen/progesterone (e.g., tamoxifen, aromatase inhibitors) is a treatment option for hormone receptor-positive breast cancer. For tumors with particular molecular markers, targeted therapy is used (e.g., HER2-positive breast cancer treated with trastuzumab). Immunotherapy: Sometimes used to treat triple-negative breast cancer [7/8.]

CHEMOTHERAPY:

Systemic chemotherapy is typically advised for high-risk individuals. There are a number of common chemotherapy methods that usually include both a taxane and an anthracycline. Doxorubicin and cyclophosphamide for four cycles, followed by paclitaxel for four cycles (AC-T) is a typical treatment plan in the US. An earlier schedule of every three weeks was outperformed by dose-dense (dd) AC-T administered every two weeks with growth factor support following each chemotherapy cycle. [9] Additional ideal AC regimens for a taxane include weekly paclitaxel for 12 weeks or docetaxel every 3 weeks for 4 cycles. [10] Although DAC, docetaxel with AC, is another common choice, it is not better than the regimens mentioned above, and docetaxel is linked to higher incidence of febrile neutropenia and greater toxicity than paclitaxel. [11]



Adjuvant chemotherapy has been shown to reduce breast cancer mortality and recurrence in meta-analyses; the benefit is greater for patients with HR negative disease. "[12]" According to Berry et al.'s analysis of trial data from the US Breast Cancer Intergroup and Cancer and Leukemia Group B, chemotherapy reduced the relative risk of cancer in patients with HR negative disease by 21-25%, while HR positive patients experienced a relative risk reduction of 8-12% [13].An estimate of the treatment benefit is provided by Oncotype DX for patients with HR positive, node-negative breast cancer. Chemotherapy decreases the risk of recurrence significantly for patients with high Oncotype recurrence scores (≥ 31) (relative risk [RR] 0.26), but it has little to no effect on patients with low scores. [14]For patients with intermediate-risk Oncotype recurrence scores, there is not enough data to make a consensus on adjuvant treatment until the TAILORx (Trial Assigning Individualized Options for Treatment) trial is completed (Figure 1). Participants in this study were randomly assigned to receive either endocrine therapy alone or endocrine therapy plus chemotherapy if their Oncotype recurrence scores were between 11 and 25. For patients in this category, chemotherapy may include regimens that contain or do not contain anthracyclines. The use of endocrine therapy alone is adequate for patients with low Oncotype recurrence scores, particularly those beneath 11. The 5-year overall survival rate for these patients using endocrine therapy alone is 98%, which is a good result. A [15]

RADIOTHERAPY:

A key part of treating breast cancer is radiation therapy, which is frequently used to lower the chance of loca recurrence following mastectomy or breast-conserving surgery (lumpectomy). It targets and destroys any remaining cancer cells using high-energy X-rays or other radiation sources.

Different Types of Radiation Therapy:

The most popular kind, external beam radiation therapy (EBRT), involves several sessions spread out over several weeks. Brachytherapy: Partial breast irradiation using internal radiation therapy with implanted radioactive sources. In certain situations, intraoperative radiotherapy (IORT) is a single dosage of radiation administered during surgery[17]

Indications:

To reduce the risk of recurrence after a lumpectomy. Post-mastectomy in individuals with high-risk characteristics (lymph node involvement, tumor >5 cm). Adverse effects: Acute: Fatigue, erythema, and desquamation of the skin. Late: heart toxicity (for left-sided breast cancer), fibrosis, and lymphedema.

Latest developments: Hypofractionation: Provides more effective dosages per fraction in a shorter amount of time. Proton therapy lowers the amount of radiation that reaches the surrounding organs[18]

ENDOCRINE THERAPY:

One of the most important treatments for hormone receptor-positive (HR+) breast cancer is endocrine therapy, sometimes referred to as hormone therapy. It inhibits tumor development and recurrence by targeting the estrogen and/or progesterone pathways.

Most individuals with HR-positive illness are advised to undergo endocrine therapy.

Endocrine therapy may be used to treat patients for five to ten years, and possibly longer.

When adjuvant tamoxifen is used for five years, the risk of recurrence is reduced by over 50% in years 0–4 and by more than 30% in years 5–9. Additionally, throughout the first 15 years, there was a 30% decrease in the annual breast cancer death rate.[19]Patients who took tamoxifen for 10 years as opposed to 5 years saw a further decrease in recurrence (by almost 25%) and breast cancer mortality (by nearly 30%) with longer medication duration, especially after year 10.The [20] The MA.17 trial shows that after 5 years of tamoxifen, an extra 5 years of aromatase inhibitors results in a 40% relative risk decrease in recurrence.[21]MA.17R showed a 34% decrease in recurrence risk after 10 years of aromatase inhibitor (AI) treatment. Individuals on 5 years of AI (some also had previously taken tamoxifen) were randomized to an additional 5 years of AI versus placebo. As a result, longer therapy sessions offer more advantages[22]

TARGETED THERAPY:

Drugs used in targeted therapy for breast cancer target cancer cells while causing the least amount of harm to healthy cells. Depending on the kind of breast cancer, it is frequently used in conjunction with immunotherapy, hormone treatment, or chemotherapy.

Various forms of targeted therapy include:

1.HER2-positive breast cancer is treated with HER2-targeted therapy. Medication: Lapatinib, Ado-trastuzumab, Emtansine, Pertuzumab, and Trastuzumab.

2.HR-positive, HER2-negative breast cancer is treated with CDK4/6 inhibitors. Medicines: Abemaciclib, Ribociclib, and Palbociclib.

3.PIK3CA mutations in advanced HR-positive, HER2-negative breast cancer. Alpelisib and Everolimus are medications.

4.PARP Inhibitors for Breast Cancer with BRCA1/2 Mutations. Medications: talazoparib and olaparib.

5.Antibody-drug conjugates, or adcs, are used to treat triple-negative and advanced breast cancer. Medication: Trastuzumab deruxtecan, Sacituzumab govitecan

IMMUNOTHERAPY:

Immunotherapy has completely changed how breast cancer is treated, especially for aggressive subtypes like triple-negative breast cancer (TNBC). Immunotherapy strengthens the body's immune system to identify and combat tumor cells, in contrast to conventional chemotherapy, which targets cancer cells directly.

Checkpoint Inhibitors:

These drugs stop the immune system from attacking tumors by blocking proteins. In combination with chemotherapy, the FDA has approved pembrolizumab, an anti-PD-1 antibody, for both early-stage and metastatic TNBC. The anti-PD-L1 antibody atezolizumab was once in use but was later taken off the market because it did not provide enough therapeutic advantages.

Antibody-drug conjugates (adcs):

ADCs give cancer cells direct access to cytotoxic medications. Sacituzumab govitecan and trastuzumab emtansine (T-DM1) have been approved for HER2-positive and TNBC, respectively, and have shown notable improvements in survival. Emerging therapies include new ADCs such as datopotamab deruxtecan, which showed encouraging clinical results and received FDA approval in 2025 for hormone receptor-positive, HER2-negative breast cancer.[26]

GENE THERAPY:

Gene therapy, which is defined as introducing genetic material into target cells via a vector to modify the gene and alter the expression of a gene's product, is another promising method for treating cancer. Targeting transcription factors, microRNA, breast cancer cells, gene editing, DNA or RNA vaccination, and other techniques are examples of gene therapy techniques. The safety and effectiveness of genetic prodrug activation treatment, which targeted the human HER-2 gene promoter, were evaluated in a Phase I clinical trial. Twelve individuals with breast cancer were enrolled in the trial, and the outcome demonstrated the safety of the method and found that up to 90% of patients had targeted gene expression.[27] Using 28 patients with metastatic TNBC, another Phase 2 trial examined the effectiveness of in situ virus gene therapy (ADV/HSV-tk) in combination with stereotactic body radiation and pembrolizumab. The results showed a 21.4% clinical benefit rate, and patients who experienced clinical benefit had long-lasting improvements in their median treatment duration (9.6 months) and overall survival (14.7 months).[2] MicroRNA's application in anti-cancer treatment also demonstrated outcomes in preventing the growth and multiplication of breast cancer cells. MRX34 is now undergoing clinical studies and, as far as we know, was one of the first miRNA replacement medications (miR-34a). For the future, it is thought to be essential in the treatment of breast cancer. Few gene therapy experiments have been published to yet, however numerous tactics have entered clinical trials in breast Cancer .[29] We summarized several clinical studies on breast cancer gene therapy in Table.1

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table 1. ongoing trials of gene therapy, vaccine, and car-t therapy of breast cancer

Identifier	Patients	Trial phase	Intervention	Endpoints
NCT00849459	mBC	Phase I	Adenovirus-mediated human interleukin-12	Serum antibodies (titer) to adenovirus, toxicity and safety
NCT00880464	Operable BC	Phase Ib	Vaccination with autologous tumor cells engineered by adenoviral mediated gene transfer to secrete GM-CS	Minimum number of vaccine doses, adverse events
NCT00505271	R/M BC	Phase I/II	Rexin-G	Clinical toxicity
NCT00673829	mBC	Phase I	Gene modified T Cells and Interleukin 2	The safety of using modified T-cells, optimal biologic dose of Interleukin 2
NCT01829971	TNBC and other cancers	Phase I	MRX34, micro RNA therapy	Maximum tolerated dose for MRX34
NCT00093834	mBC	Phase I	Allogeneic GM-CSF-Secreting Breast Cancer Vaccine	Toxicity of vaccine
NCT00784524	mBC	Phase II	LMI Vaccination + IL-2	Disease response
NCT04674306	IIA-IIIC TNBC	Phase I	α-lactalbumin vaccine	Treatment cohort maximum tolerated dose of α-lactalbumin vaccine
NCT04430595	III–IV BC	Phase I/II	4SCAR T cells	Number of patients with adverse events
NCT02792114	mBC	Phase I	Mesothelin-targeted T cells	Maximum tolerated dose

Abbreviations: BC, breast cancer; mBC, metastatic breast cancer; R/M, recurrent/metastatic; TNBC, triple negative breast cancer; CAR-T, chimeric antigen receptor T.

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CONCLUSION AND FUTURE PERSPECTIVE:

It is commonly known that both systemic and local medicines are beneficial in treating breast cancer. The standard of care for early-stage breast cancer is surgery-based systemic and local therapies. Chemotherapy-based systemic treatments are still the best option for metastatic breast cancer, and surgery is only utilized as palliative therapy in a small number of patients. However, the advantages of conventional treatment methods for survival were minimal. The development of immunotherapy and targeted therapy further altered the way that early and metastatic breast cancer are treated. The FDA has approved atezolizumab or pembrolizumab in combination with chemotherapy as the first-line treatment for metastatic TNBC that is PD-L1 positive. Neoadjuvant Pembrolizumab, an adjuvant, is also authorized for early TNBC. Clinical trials for a number of new ICIs and ICIbased combination therapies have begun. Furthermore, a number of cutting-edge treatments for breast cancer are being researched, including gene therapy, vaccines against the disease, adoptive cell therapies, such as T cell receptor therapy and CAR-T therapy, and others.

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