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Beyond the Lump: Unravelling Breast Cancer's Pathological features and Therapeutic Horizon

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ABSTRACT

Breast cancer is one of the world's most frequent and lethal tumours, accounting for a significant amount of cancer-related morbidity and fatality or death rate, particularly among women. Although initial stages of breast cancer may be curable, timely identification and suitable therapy are not routinely available. This discrepancy in healthcare access, particularly in low- and middle-income nations, has a continued influence on survival rates and quality of life. As our understanding of the biology associated with breast cancer grows, the illness is increasingly seen as a diverse set of diseases with discrete molecular subtypes, each with its own prognosis and treatment implications. This study provides a comprehensive overview of breast cancer, beginning with its pathophysiology and categorization systems and proceeding through the landscape of both traditional and innovative therapeutic options. Surgery, chemotherapy, and radiation therapy remain standard treatments, but recent breakthroughs have extended therapeutic choices with the advent of targeted medications. Therapies including HER2 inhibitors, CDK4/6 inhibitors, PARP inhibitors, and immune checkpoint inhibitors have considerably improved clinical outcomes in some patient groups. Furthermore, hormonal medicines and gene-based treatments are evolving, enabling more personalized and effective care regimens. This article seeks to provide a comprehensive overview of how breast cancer is being handled and where it is going by investigating both existing therapies and the most recent advances in care.

Keywords: Breast cancer, Molecular subtypes, Targeted therapy or treatment, HER2 inhibitorsCDK4/6 inhibitors, PARP inhibitors, Immunotherapy, Personalized medicine

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INTRODUCTION

Breast cancer is one of the three most frequent malignant cancers globally. Initial stages of breast cancer are thought to be possibly treatable. Therapy has advanced significantly in recent years, with a decrease in intensity for both locoregional and systemic drug therapy; avoiding overtreatment as well as under treatment has become a primary emphasis [1]. The goal of increasing or improving breast cancer outcomes through prompt detection, diagnosis, and care has proven challenging to achieve in underdeveloped nations due to resource and infrastructural limitations. [2]. The World Health Organisation (WHO) states that the cornerstone of breast cancer legislation continues to be increasing of improving breast cancer outcomes and survival via early diagnosis. Breast cancer is treated using a variety of contemporary drugs. For those who are at a higher risk of developing breast cancer, medical therapy with antioestrogens like raloxifene or tamoxifen may prevent the disease. [3]. Traditional therapies including surgery, chemotherapy, and radiation have considerably increased survival rates, but they frequently cause severe toxicities and drug resistance. In recent decades, targeted drug molecules have transformed breast cancer treatment by precisely blocking oncogenic pathways while minimising systemic adverse effects [4]. The development of targeted medicines such as HER2 inhibitors (Trastuzumab, Pertuzumab, Tucatinib), CDK4/6 inhibitors (Palbociclib, Ribociclib, Abemaciclib), PI3K inhibitors (Alpelisib), and PARP inhibitors (Olaparib, Talazoparib) has dramatically improved results in specific patient populations [5,6]. Furthermore, the introduction of antibody-drug conjugates (ADCs) such as Sacituzumab (Govitecan) and the administration of immune checkpoint inhibitors (Pembrolizumab, Atezolizumab) in triple negative breast cancer has broadened the treatment landscape [7]. Despite these gains, some problems remain, such as primary and acquired drug resistance, diverse tumour development, high treatment costs, and restricted access to innovative medicines in resource-constrained areas [8].

Pathophysiology

Understanding the genesis, course, and response to treatment of breast cancer requires knowledge of its pathophysiology and molecular subtypes. Better patient outcomes, tailored treatment, and targeted medication development are all aided by this understanding. Breast cancer patients' quality of life and survival rates are enhanced by tailored treatment plans made possible by the identification of subtypes [9]. A person's genetic predisposition and external environmental influences interact intricately to cause breast cancer. Normal cells divide as many times as necessary before stopping. They attach to other cells and can stay in tissues for a long period. When cells lose the capacity to stop proliferating, attach to other cells, and die at the proper time, they eventually become cancerous. Cells are protected from programmed cell death by a variety of proteins and processes. One of the protective routes is the PI3K/AKT pathway, while another is the RAS/MEK/ERK pathway. When a cell is preparing for apoptosis, the PTEN protein often inhibits the PI3K/AKT pathway. In certain breast tumours, the PTEN protein gene is metamorphosed, trapping the PI3K/AKT pathway in the "on" state and preventing the cancer cell from self-destructing [10]. Most breast cancers are sporadic (90%-95%), with just 5% to 10% of individuals having a known genetic mutation. BRCA 1 and 2 are the most often related genetic disorders. Invasive ductal carcinoma and invasive lobular carcinoma are the most frequent pathologic types of invasive breast cancer. Carcinogenesis results from a complex interaction of genetic predisposition and environmental risk factors, hormonal factors, and patient-related variables. The development, therapy, and prognosis of breast cancer are intimately related to the following molecular subtypes:

- **Luminal A**: Human epidermal growth factor receptor (HER)-2 negative, hormone receptor positive
- **Luminal B**: Hormone receptor-positive, Human epidermal growth factor receptor (HER-2) positive
- **Basal-like**: Hormone receptor and Human epidermal growth factor receptor (HER-2) negative
- **HER-enriched**: Human epidermal growth factor receptor (HER-2) positive, hormone receptor-negative [11].

BC often begins with duct hyperplasia and progresses to benign tumours and even metastatic malignancy when carcinogens activate them. The microenvironment of tumours, such as macrophages, and the effect of stroma both play important roles in the genesis and progression of BC. Macrophages can create a mutagenic inflammatory milieu, which promotes angiogenesis and permits cancerous cells to escape via immune system rejection. The start and progression of BC can be explained by the stochastic and cancer stem cell concepts. The stochastic theory states that single cells type a differentiated progenitor or stem cell is the source of every cancer subtype. Any breast cell can gradually develop random mutations that, if sufficient, can turn the cell into a cancerous one. All tumour subtypes are created by the same progenitor cells, or stem cells, according to the cancer stem cell theory. Genetic and epigenetic alterations in progenitor or stem cells will produce distinct cancer phenotypes [12].

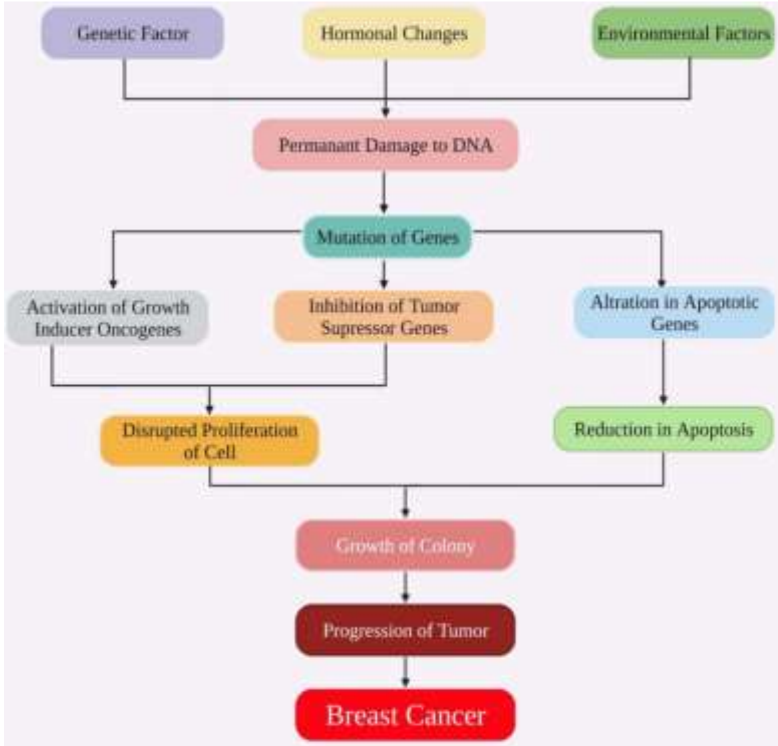

Figure 1: Cancer stem cell theory [13]

Classification of breast cancer (types)

Breast cancer can be categorized according to its histological type, molecular subtype, and invasiveness. Here's the breakdown:

Based on Invasiveness

- **<u>Non-Invasive (In Situ) Breast Cancer:</u>**

  Ductal Carcinoma in Situ (DCIS): Cancer cells are confined to the milk ducts and haven't spread [14].

  Lobular Carcinoma in Situ (LCIS): Abnormal cells are found in the lobules are considered a risk factor rather than actual cancer [14].

- **<u>Invasive (Infiltrating) Breast Cancer:</u>**

  Invasive Ductal Carcinoma (IDC): Most common type (~80% of patients); starts in the milk ducts and spreads to the surrounding organs [15].

  Invasive Lobular Carcinoma (ILC): Starts in the lobules and spreads, often harder to detect than IDC [15].

Based on Molecular Subtype (Receptor Status & Genetic Profile)

<u>Hormone Receptor-Positive (HR+) Breast Cancer:</u>

Both progesterone receptor-positive (PR+) and oestrogen receptor-positive (ER+) are present. more prevalent and reacts favourably to hormonal treatments (such as aromatase inhibitors and tamoxifen) [16].

HER2-Positive Breast Cancer:

HER2 protein overexpression, which causes tumour development to become more aggressive. This subtype responds well to targeted treatments such as pertuzumab and trastuzumab (Herceptin) [17].

Triple-Negative Breast Cancer (TNBC):

It is more aggressive and more difficult to treat since it lacks ER, PR, and HER2 receptors. limited alternatives for treatment, frequently treated with immunotherapy and chemotherapy [18].

Triple-Positive Breast Cancer:

A combination of hormone therapy and targeted therapy is one of the several therapeutic choices available to those who test positive for ER, PR, and HER2 [17].

Rare types of Breast Cancer

Inflammatory Breast Cancer (IBC):

A rare and aggressive type characterized by swelling, redness, and peau d'orange (skin dimpling). Often misdiagnosed as an infection and requires urgent treatment [18].

Paget's Disease of the Breast:

Affects the nipple and areola and is often seen with underlying DCIS or invasive carcinoma [16].

Metaplastic Breast Cancer:

A rare form of breast cancer with mixed cell types, often more aggressive than typical IDC [15].

Medullary, Mucinous, and Tubular Carcinomas: Less common, but generally have a better prognosis than typical IDC [16].

TRADITIONAL TREATMENT APPROACHES

Surgical treatment

Lumpectomy

Breast-conserving surgery is also referred to as many terminologies, such as quadrantectomy, lumpectomy, and partial mastectomy. These phrases differ somewhat in approach but have the objective of breast preservation. Non-palpable tumours necessitate the use of image-guided localization methods, as detailed in the equipment section above. Quadrantectomy entails removing the tumour, including a 2- to 3-m margin, the pectoralis fascia, and the underlying skin. A lumpectomy, on the other hand, refers to a smaller tissue excision with a 1 cm border 20. For stage I and stage II breast cancer, TM was compared to lumpectomy, with or without radiation therapy, in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B 06 study. The disease-free, distant disease-free, and overall survival rates following lumpectomy, with or without radiation therapy, were similar to those following TM at five and eight years of follow-up. However, the lumpectomy group that did not receive radiation therapy had a higher chance of ipsilateral breast cancer recurrence, also known as in-breast recurrence [21].

Mastectomy

Mastectomy has become a more sophisticated surgery, with several options available. One alternative is traditional mastectomy, which is appropriate for certain individuals. This approach is frequently used as an outpatient treatment because to its short recovery time and minimal risk of complications. For certain individuals, subcutaneous mastectomy with rapid reconstruction may be a better alternative. This procedure includes removing breast tissue along with the tumour while keeping the skin flaps intact for quick repair. Autologous tissue or a prosthetic implant can be used for reconstruction.

Before surgery, patients should have a full consultation to understand their options and the procedures involved. For implant-based reconstruction, there are two options:

1. A permanent prosthesis with a defined size and form requires only one surgical surgery.
2. A tissue expander is gradually inflated to attain desired breast volume, followed by a permanent implant.

The final choice may need to be made during surgery in some circumstances, and both the patient and the surgeon must weigh the advantages and disadvantages of these options.

Implant Placement: Pre-Pectoral vs. Sub-Pectoral

A critical part of implant-based repair is deciding whether the implant should be put in front of (pre-pectoral) or behind (sub-pectoral) the pectoral muscle. Traditionally, implants were placed below the muscle to offer extra support and covering. However, direct comparisons between these treatments are limited since surgical procedures and equipment have evolved greatly over time. Recent research of 91 patients found that subpectoral implantation was advantageous. However, this study was conducted in 1981, and surgical developments since then have resulted in superior procedures. A more recent 2018 research comparing the two techniques discovered that pre-pectoral implant insertion resulted in reduced postoperative pain, faster recovery from upper extremity functional impairment, superior cosmetic outcomes (measured by BREAST-Q scores), and cost savings [22-24].

Radiation therapy

For both patients having a mastectomy and those undergoing breast conservation, radiation therapy (RT) is an essential part of the treatment for breast cancer. While post-mastectomy radiation therapy has been demonstrated to improve survival in individuals who are carefully selected, studies evaluating breast-conserving therapy have demonstrated the benefits of adjuvant radiation treatment in terms of both local control and breast cancer mortality [25]. One of the most important oncologic treatments for patients with breast cancer undergoing mastectomy or breast-conserving surgery is post-operative radiation therapy (RT). Conventional doses of radiation are between 50 and 50.4 Gy and are usually administered in 25-28 fractions over 5-6 weeks in accordance with a prescribed schedule. The incorporation of this historical regimen into clinical practice was motivated by the notion that a cumulative dosage of more than 50 Gy, administered in 1.8-2.0 Gy fractions, offers tumour control while limiting injury to normal tissue. This is because breast cancer has historically been thought to be less sensitive to dosage changes per fraction than healthy normal tissues that restrict dosage, and because classical radiobiology has a better grasp of the dosages required to treat subclinical illness [26]. Hypo fractionated plans decrease the total treatment time by lowering the number of fractions, making the therapy plan more convenient for patients and healthcare providers. Hypofractionation may also enhance patients' access to medical care (particularly in cases where capacity is restricted), minimize indirect expenses associated with work disruptions and travel to the radiation oncology department, and lower direct treatment expenditures [27]. According to recent studies, late cardiac damage following breast cancer treatment may be influenced by even modest radiation exposures to the heart. Coronary artery disease (CAD), congestive heart failure (CHF), pericardial disease, valvular heart disease, conduction problems, and sudden cardiac death can all be brought on by radiation exposure to the heart [28, 29].

Chemotherapy

Neoadjuvant therapy may be indicated before to surgery for early invasive breast cancer, whereas adjuvant treatments may be recommended post-operatively. These therapies can lower breast cancer recurrence and mortality, but they may also raise the chance of deaths from other conditions [30]. Breast cancer is treated using a multimodal approach that involves neoadjuvant chemotherapy, surgery for operable tumours, radiation, adjuvant chemotherapy, and/or endocrine therapy. Neoadjuvant therapy is the primary treatment for locally advanced and inoperable breast cancer. Systemic neoadjuvant treatment can decrease tumours and make previously incurable cancers operable [31]. Neoadjuvant chemotherapy is now widely used in early-stage breast cancer (EBC) and locally advanced BC because it increases the likelihood of breast-conserving surgery (BCS) by downstaging the illness and assessing tumour response to therapy [31]. Neoadjuvant chemotherapy is gaining popularity in the treatment of breast cancer and is now considered the standard of care for triple negative and high-risk breast tumours that express Human Epidermal Growth Factor

Receptor. The advantages of the neoadjuvant approach extend beyond the pathological full response to tumour down staging, which permits conservative breast and axillary surgical options. Response evaluation offers useful prognostic data for adjuvant therapy escalation and de-escalation to maximize oncological results. Neoadjuvant chemotherapy is now frequently employed in the treatment of breast cancer, and clinical decision making necessitates a thorough histological examination as well as an understanding of molecular tumour biology [32]. Chemotherapy in British Columbia may involve the use of early neoadjuvant chemotherapy before the start of adjuvant chemotherapy after appropriate surgical treatment and/or radiation. Neoadjuvant chemotherapy can be given in a combination setting. A combination of docetaxel and epirubicin was tested for safety and efficacy in women with inflammatory breast carcinoma and big, operable, or locally progressed (Stage III) breast cancer in phase II neoadjuvant research. The response rate from the experiment was 76.7%. A third of patients experienced febrile neutropenia, 80% experienced grade 4 neutropenia, and over 25% experienced clinically severe diarrhoea. Prophylactic haemopoietic growth factor support was then used, enabling patients to complete their intended course of treatment. Neoadjuvant treatment of epirubicin plus docetaxel was found to be both practical and successful for patients with breast cancer, including those with unfavourable clinical presentations or signs and symptoms including inflammatory and locally progressed breast cancer. [31, 33]. One research found that combining four cycles of preoperative docetaxel with four cycles of preoperative doxorubicin and cyclophosphamide significantly enhanced the clinical and pathologic response rates for operable breast cancer [34]. Chemotherapeutic drugs alone (at least two chemotherapeutic agents) or in combination with hormone therapy or immunotherapy are examples of adjuvant breast cancer treatment combinations.[31]. The addition of an alkylating drug (cyclophosphamide) and antimetabolites (methotrexate and 5-fluorouracil) to breast cancer therapy produced better outcomes (a significant reduction in the likelihood of recurrence), according to data from the Istituto Nazionale Tumori in Milan, Italy. [31, 35]. In a prospective clinical research, cyclophosphamide, methotrexate, and 5-fluorouracil (5-FU) (CMF regimen) was the first adjuvant chemotherapy combo treatment examined. The Istituto Nazionale Tumori in Milan, Italy, started the study in 1973. Node-positive patients who had undergone radical mastectomy were randomly assigned to receive 12 cycles of CMF once every 28 days (cyclophosphamide: 100 mg/m2 orally on days 1-14; methotrexate: 40 mg/m^2 IV on days 1 and 8; and 5-fluorouracil: 600 mg/m^2 IV on days 1 and 8) or no further treatment. According to the 342-month follow-up updated report, CMF outperformed the control group (no additional medicine) in terms of overall survival (OS; HR, 0.79; P = 0.04) and disease-free survival (DFS; hazard ratio (HR), 0.71; P = 0.005).[35]. When treating breast cancer, chemotherapy combinations often include taxanes, a large class of cytotoxic medications. Since their introduction in the 1990s, they have become some of the most successful chemotherapeutic medications used to treat breast cancer [36]. Clinical studies for the first drug in the family, paclitaxel, started in the early 1980s. In response to the initial shortage and issues in producing paclitaxel, docetaxel, another member of the class, was eventually created and made available. The evaluation of paclitaxel in combination with other cytotoxic agents for MBC treatments began with the concurrent initiation of phase I clinical trials of paclitaxel/doxorubicin combinations by the University of Texas M. D. Anderson Cancer Centre and the National Cancer Institute's Medicine Branch (USA) [31].

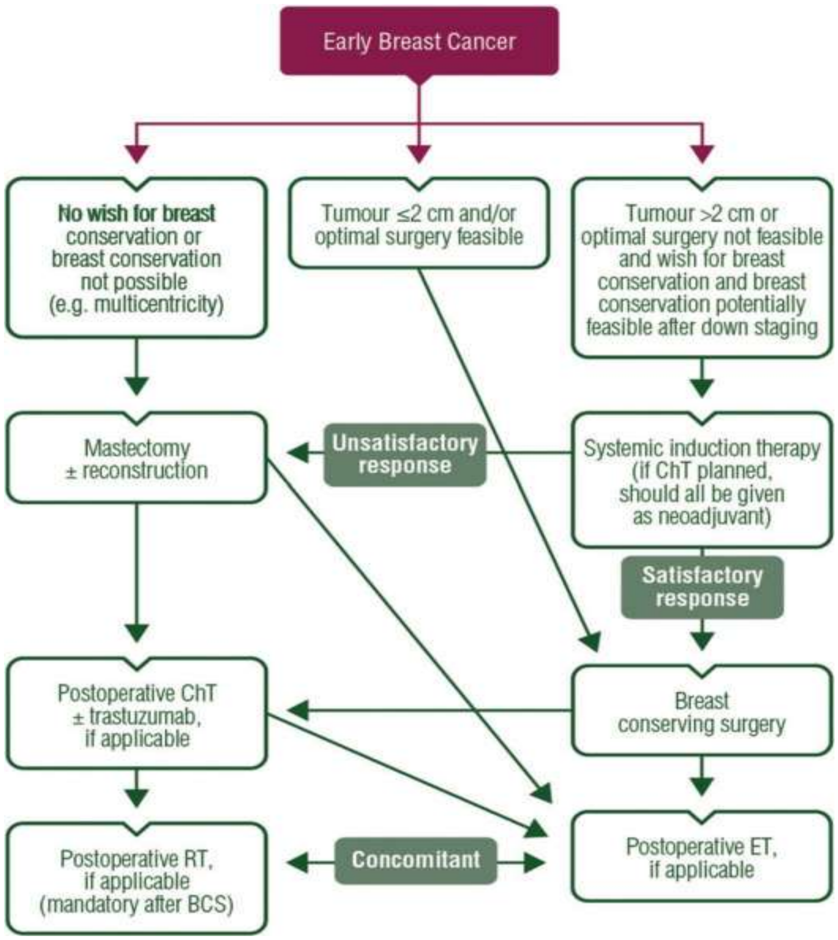

Figure 2: Early Breast Cancer[37]

Novel and emergent treatments

Targeted therapy

Targeted therapies for breast cancer have improved dramatically during the last two and a half decades. This has been accomplished due to expanded understanding of the aetiology of breast cancer formation as a consequence of various individual research studies and large-scale efforts such as The Cancer Genome Atlas (NCI/NIH) [38]. Human epidermal growth factor receptor 2

(HER2) is a kind of tyrosine kinase receptor that regulates cell proliferation, survival, differentiation, angiogenesis, invasion, and metastasis. HER2 heterodimerization with the Epidermal Growth Factor Receptor (EGFR/HER1) results in tyrosine phosphorylation, which initiates a mitogenic response. They discovered HER2 amplification in 53/189 (28%) of the initial human breast tumours examined, which was linked with an increased risk of recurrence and death. These findings provided a solid foundation for developing anti-HER2 medications. Trastuzumab, a humanized monoclonal antibody directed at an extracellular epitope on HER2, was the first of these medications to be developed and authorized for clinical use. Trastuzumab binding to HER2 results in receptor down regulation, which decreases proliferation and survival in HER2-overexpressing cancer cells [38]. Chemotherapy with trotuzumab significantly improved overall quality of life in H0648g (n = 400) when compared to treatment (51% vs. 36%; P <.05). When compared to baseline in both trial groups, the chemotherapy-plus-trastuzumab arm demonstrated a significant reduction in fatigue at week 32 (chemotherapy finished at week 20) (P <.05). Additionally, more patients in the group receiving chemotherapy with trotuzumab shown improvements in their role-playing and physical functioning. Throughout all time periods, the subscale scores in H0649g (n = 154) and H0650g (n = 74) stayed constant. From week 12 to week 36, clinical responders in H0649g demonstrated significant gains (>or= 10 points) in each of the five subscales. All subscale scores significantly decreased for nonrespondents. By week 12, clinical responders in H0650g shown notable gains in global QOL, social and role functioning, and nonresponse's scores on all subscales. [39]. Poly (ADP-ribose) polymerases (PARPs) are enzymes that repair single-stranded DNA breaks, primarily via the base excision repair pathway. When PARPs are inhibited, these single-strand breaks remain unrepaired and can eventually evolve to double-strand breaks. In such cases, cells increasingly rely on a backup repair technique called homologous recombination to heal the damage. PARP inhibitors are highly effective in malignancies including BRCA1 or BRCA2 gene mutations, which are required for homologous recombination. If cancer cells lack functioning BRCA proteins, they are not able to properly repair DNA damage, which therefore leads to cell death [40]. In a phase 3 double-blind, randomized research, oral olaparib or a placebo was administered for a year after standard therapy to patients with germline BRCA1/2 mutations and HER2-negative early breast cancer. The primary outcome was invasive disease-free survival. In patients with high-risk, HER2-negative early breast cancer with germline BRCA1/2 mutations, adjuvant olaparib improved both distant disease-free survival and invasive survival [41]. The ABRAZO (NCT02034916) phase II study tested talazoparib (1 mg/day) for advanced breast cancer patients with germline BRCA mutations. Cohort 1 had previous platinum response, while Cohort 2 got ≥3 non-platinum regimens. Independent assessment established the primary endpoint as objective response rate. Talazoparib had good anticancer efficacy in individuals with metastatic breast cancer and the germline BRCA mutation [42]. Oral CDK4/6 inhibitors such as palbociclib, ribociclib, and abemaciclib have enhanced the treatment of hormone receptor positive, HER2 negative metastatic breast cancer. Abemaciclib is approved as a first-line treatment in conjunction with aromatase inhibitors or fulvestrant, while ribociclib has been shown to enhance disease-free survival in stage II or III early breast cancer. While these drugs have generally high safety ratings, their distinct hazard profiles demand attentive patient counselling. This study investigates CDK4/6 inhibitor-related adverse events, risk factors for intolerance, and safety concerns in specific groups such as the elderly and those with renal impairment in order to optimize patient management [43].

Immune checkpoint inhibitors

Treatment for a number of malignancies that have spread to the brain has changed thanks to immune checkpoint inhibitors (ICIs). Real-world data show that non-small cell lung cancer (NSCLC) and melanoma have intracranial consequences, with similar reactions in brain and visceral metastases. In breast cancer, the most encouraging results and immunotherapy indications are now limited to a subgroup of patients with TNBC. Investigating current research on immunotherapy and CNS metastatic disease and its potential use to BCBM, particularly TNBC, is the aim of this study [44]. Pembrolizumab, a humanized monoclonal IgG4-κ antibody, specifically targets PD-1 with high affinity and selectivity. Pembrolizumab has been approved by several countries to treat advanced melanoma. Furthermore, in a number of advanced malignancies, including urothelial carcinoma, head and neck cancer, gastric cancer, and non-small-cell lung cancer (NSCLC), pembrolizumab clinical studies have demonstrated intriguing effectiveness with long-term responses and a tolerable safety profile [45]. For patients with significantly pretreated, advanced TNBC, this phase 1b study provides first indications of clinical benefit and a potentially acceptable safety profile for pembrolizumab given every two weeks [45].

Hormonal therapy

Hormonal treatment is essential for all patients with hormone receptor-positive breast cancer. It works in both adjuvant and metastatic illnesses [46]. Multiple lines of evidence suggest a link between oestrogen and breast cancer. Tamoxifen, selective oestrogen receptor (ER) modulators (SERMs), fulvestrant (SERD), and aromatase inhibitors all lower the risk of recurrence or progression in people with ER-positive breast cancer. Antioestrogens such as tamoxifen and aromatase inhibitors have been shown to reduce risk of breast cancer by decreasing ER signalling.

Furthermore, excessive blood oestrogen levels have shown a greater risk of breast cancer. Breast epithelial cell proliferation increases in postmenopausal women taking oestrogen-containing hormone replacement treatment, as well as in mice and primates treated with oestrogen, proving that oestrogen contributes to the development of breast cancer [47]. Current data supports oestrogen's overall oncogenic and tumour-promoting role in breast cancer risk, recurrence, and growth/progression [47]. SERDs are primarily oestrogen receptor antagonists, in contrast to tamoxifen (SERM). By blocking the oestrogen receptors (ERα) α isoform, SERDs cause a conformational shift that inhibits dimerization and encourages proteasome-mediated destruction. Proliferative gene synthesis and translocation to the nucleus are slowed as a result [48].

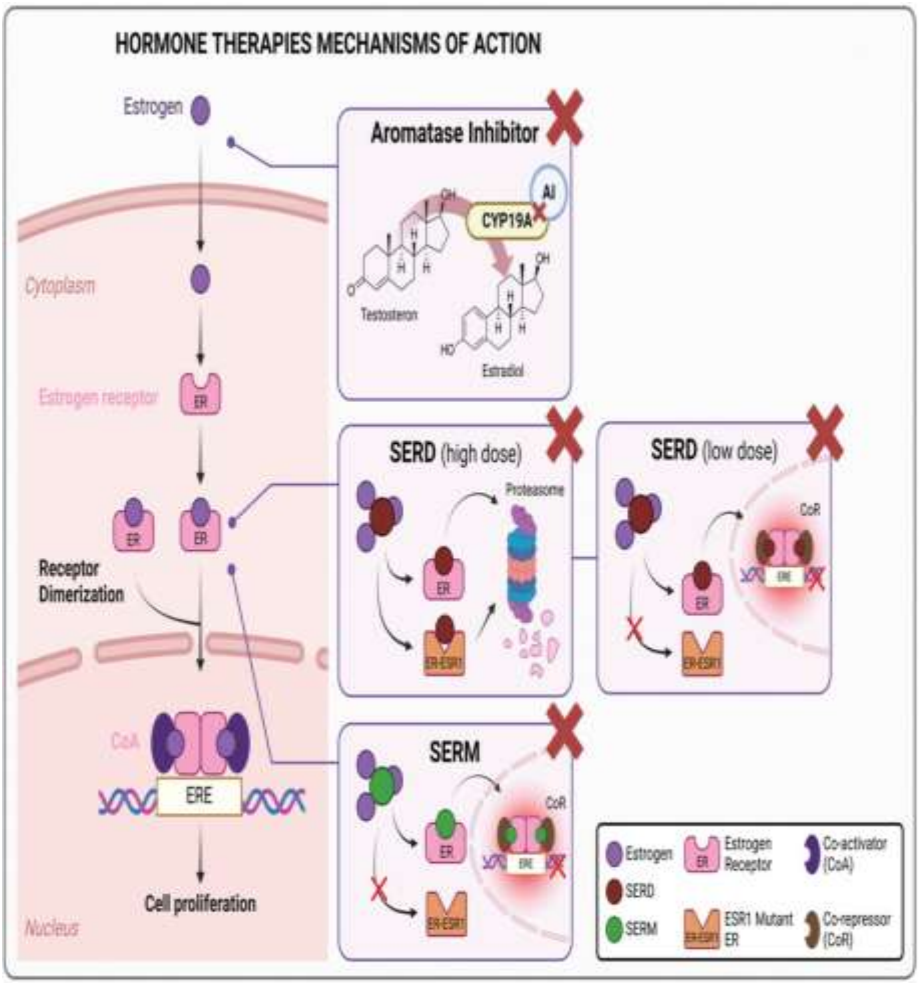

Figure 3: Hormonal therapy mechanism[48]

Gene therapy

Genetic changes that caused certain breast cells to become abnormal were connected to each subtype of breast cancer. For breast cancer subtypes with a variety of genetic aberrations, gene therapy is therefore a potential therapeutic option. Breast cancer susceptibility genes, such as BRCA1 and BRCA2, tumour protein p53 (TP53), phosphatase and tensin homologue (PTEN), serine/threonine kinase 1 (STK11), and cadherin 1 (CDH1), have high-risk variant alleles that affect the relative risk of breast cancer. Treatment possibilities for breast cancer gene therapy include gene editing, gene repair, gene suppression, and suicide gene therapy.[49]. Gene therapy has emerged as a successful treatment for breast cancer as a result of research into the molecular causes of the illness. The technique of inserting genetic material into target cells via a vector and then correcting, adding, or suppressing those genes is known as gene therapy. The capacity to target cancer cells while avoiding healthy ones is necessary for this strategy. Furthermore, clinical trials have demonstrated that this technique is less harmful than standard medicines [50].

CONCLUSION

Breast cancer management has progressed significantly from traditional therapy paradigms to precision-guided treatments that use molecular insights. The combination of targeted medicines with immunotherapy has increased survival rates and quality of life for many patients, particularly those with aggressive subtypes such as HER2-positive and triple-negative breast cancer. Despite these advances, obstacles like as medication resistance, restricted treatment access in resource-constrained regions, and tumour heterogeneity persist. Future efforts should focus on increasing the availability of novel therapies, enhancing early detection systems, and doing further research into resistance mechanisms. Finally, a multidisciplinary, individualized treatment plan is critical to improving outcomes in breast cancer care.

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