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Review Article

Targeting the Tumor: Molecular Pathways and Therapeutic Frontiers in Breast Cancer

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ABSTRACT

Breast Cancer (BC) is the leading cause of mortality in the majority of women around the globe. It stands as one of the most common types of cancer after non-melanoma skin cancer. Contemporary oncology distinguishes BC utilizing molecular markers into three subtypes – invasive, non-invasive, and metastatic, out of which invasive ductal carcinoma is the most common. These subtypes of BC are determined by their assessment of hormone receptors (ER/PR), HER2 status, and proliferation biomarkers (Ki-67), which directs therapeutic decision-making in context of the treatment to be provided to the patient. Prevalent Signature biomarkers help detect the type of BC, the stage, and its status (benign or metastatic), the treatment to be provided, and targeted therapeutics to cure and prevent its recurrence. Oncogenesis in breast cancer is a result of aberrant and disrupted signalling pathways. Novel therapies are designed to reduce the risk of cancer providing a prolonged survival. Understanding the molecular mechanism can help aid the desired therapeutics for the next generation with more focus on reducing the toxicity and enhancing the efficacy of the drugs administered. This review aims to provide a collaborative preview of the signaling pathways utilized in breast cancer, precision medicine in oncology and targeted or combined therapeutics as emerging innovative treatment for the upcoming generations.

Keywords: Cancer, Molecular markers, Oncogenesis, Precision medicine signaling pathways, Therapeutics.

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INTRODUCTION

Breast cancer is a disease where cells begin to grow uncontrollably and form a tumor and is one of the most common types of cancer. In accordance with the latest database of global cancer, breast cancer percentage is now 11.7% of new cancer cases in 2020, overtaking lung cancer as the most prevalent cancer globally (Xiong *et al.*, 2025; Sung *et al.*, 2021). At the time of diagnosis, approximately 90 percent of breast cancers are rarely metastatic (Waks *et al.*, 2019). Based on the presence or absence of the molecular signatures of the human epidermal growth factor two (HER 2) (Carvalho *et al.*, 2025; Waks *et al.*, 2019), they are categorised into three subcategories: invasive, non-invasive, and metastatic. The therapeutic target for patients having benign tumors is to eradicate the tumor and prevent its resurgence. Over the past few years, significant strides have been achieved in the ongoing pursuit of novel therapies to treat breast cancer (Tong *et al.*, 2018). Subtypes of Breast cancer include Human receptor (positive HR+ (Human Receptor Positive), Human epidermal growth factor HER2+, Triple Negative Breast Cancer (TNBC), Triple positive breast cancer, Luminal A BC, B BC, HER2-enriched, Basal-like like and Claudin-Low. All Breast cancer variants are regularly exposed to chemotherapy, radiation therapies, immunotherapy, hormonal therapy, and targeted therapies in conjunction with surgery (Burguin *et al.*, 20121). Factors that influence the type of therapy involved depend on the stage of cancer, HER2 status, and Ki-67 marker (a key indicator of how fast cancer cells proliferate). For non-metastatic breast cancer, surgery-based recuperation is the conventional practice, and chemotherapy-based pre-emptive systemic therapy can reduce the size of the tumor of the breast, making preserving breast tissue viable, and eliminating the requirement for dissection of axillary lymph nodes (Wang *et al.*, 2023). Current breast cancer treatments are induced by their molecular characterisation, thus employing more targeted therapies and molecular pathways to treat the root cause. For instance, the gene encoding the transmembrane tyrosine kinase receptor *ERBB2* resides in chromosomal band 17q12 (Bertucci *et al.*, 2024). Upregulation of the gene *ERBB2*

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is an indication of the tumorigenesis of the mammary tissues (Figure 1). To identify the precise targeted therapy, it is crucial to determine the progress of the *ERBB2* gene, which is determined by the Immunohistochemistry (IHC) on tissue segments and the Fluorescence *in situ* Hybridisation (FISH) on interphase chromosomes (Bertucci *et al*., 2024). Drugs such as trastuzumab, often marketed as Herceptin, which substantially hampers HER2 signalling, induce the *ERBB2* gene to respond (Figure 1). It binds to HER2, causing the induced signals to be blocked that tell the cancer cells to grow and proliferate. Another important class of targeted therapy is endocrine therapy, which works by blocking the growth-stimulating effects of Estrogen via ER (Gil *et al*., 2014). Thus, in developing more targeted therapies, understanding the molecular pathways is essential to identify targeted therapies for any altered molecular pathway. Key molecular pathways include Estrogen-Receptor pathway (ER pathway), Progesterone pathway, DNA damage response pathway, notch and hedgehog pathway, PI3K/AKT/mTOR Pathway, and CDK4/6-RB pathway. Future treatment regimens that integrate immune treatments and cancer stem cell-targeted therapies elevate the possibility of effectively curing a greater percentage of women with severe and resistant metastatic complications (Toss *et al*., 2015). This review analyses breast cancer, with emphasis on its epidemiology, advancements in precision oncology through specialized therapies, and innovative emerging treatment approaches under consideration to shape future trends in breast cancer.

Key Molecular Pathways in Cancer

Molecular pathways modulate cellular growth and proliferation, which are recurrently dysregulated during oncogenesis and tumor progression. Studies suggest that Preclinical and clinical studies conclude that precise therapies can induce tumor regression, obstruct disease progression, and, in specific acknowledged cases, prolong survival in cancer patients with evolved malignancies (Press *et al*., 2007). Several pathways of breast cancer are discussed below.

Growth Factor Signalling Pathways

Epidermal Growth Factor Receptor /Human Epidermal Growth Factor2 Pathway EGFR/HER2

The Epidermal Growth Factor Receptor (EGFR) and Human Epidermal Growth Factor Receptor 2 (HER2) signalling pathways are crucial signalling cascades for cell growth, survival, and proliferation. Recurrent dysregulation initiates oncogenesis and tumor progression. EGFR binds with EGF and undergoes dimerization, frequently heterodimerizing with additional receptor family members following tyrosine phosphorylation, leading to abnormal cellular proliferation (Rubin *et al*., 2024; Seshacharyulu *et al*., 2012). Overexpressed EGFR induces malignant transformation by stimulating pro-tumorigenic processes, including uncontrolled proliferation, anti-apoptotic properties, and metastasis key pathological features of oncogenesis and tumor progression (De Larco *et al*., 1980; Sebastian *et al*., 2006). Several anti-EGFR therapies fall under the class of targeted cancer treatments that block the effect of EGFR, thus inhibiting cell growth. These anti EGFR drugs can be administered through monoclonal antibodies or Tyrosine Kinase Inhibitors (TKIs). ErbB (HER) receptors are expressed in epithelial, mesenchymal, and neuronal tissues and are essential for multiple specialized cellular functions, including proliferation, differentiation and programmed cell death (apoptosis) (Olayioye *et al*., 2001). Overexpression of the Human Epidermal Growth Factor 2 is associated with aggressive breast cancers and poor prognosis. Anti-HER2 drugs such as trastuzumab, also known as Herceptin, a monoclonal antibody, used in the treatment of metastatic breast cancer. Lapatinib, a kinase inhibitor and an orally active anti-cancer drug, also blocks the tyrosine kinases of HER1 and HER2 (Stanowicka-Grada *et al*., 2023). By the introduction of anti-HER2 drugs, patient-reported outcomes have achieved superior results relative to HER2-negative disease (Stanowicka-Grada *et al*., 2023). Certain antibody drug conjugates are also administered in the body along with chemotherapy for prolonged survival and to prevent the recurrence of the cancer. Current antibody-drug conjugates approved are Trastuzumab Emtansine (T-DM1) and Trastuzumab Deruxtecan (T-DXd) (Zhu *et al*., 2024).

PI3K/AKT/mTOR pathway

The Phosphatidylinositol 3-kinase (PI3K), Protein kinase B (AKT), and mammalian Target of Rapamycin (mTOR) or the PI3K/Akt/mTOR pathway modulates several regular cellular processes, such as growth, survival, proliferation, and motility, dysregulation of which is vital to carcinogenesis (Morgensztern *et al*., 2005). P13K is a lipid kinase that phosphorylates PIP2 (4,5-bisphosphate) to phosphatidylinositol (3,4,5)-trisphosphate (Miricescu *et al*., 2021). Once phosphorylated, it creates a docking site for AKT (protein kinase B) to bind. Akt, when phosphorylated, regulates multiple targets, including mTOR, a pivotal signalling cascade that induces oncogenesis by combining diverse protein interactions (He *et al*., 2021). The Forkhead box transcription factors (FOXO) are a subdivision of the FOX family and are a vital protein in the PI3K/AKT pathway. Through phosphorylation-induced FOXO inactivation, which interferes with the control of oncogenes such as AR, ERG, and Runx2, the oncogenic PI3K/Akt cascade leads to tumorigenesis (Greer *et al*., 2008; He *et al*., 2021). Mammalian target of rapamycin (mTOR) indulges in several bodily signalling pathways to control cell division, autophagy, and cell death (Zou *et al*., 2020). Dysregulation in the PI3K/AKT/mTOR leads to active tumor formation and therapeutic escape from antineoplastic therapies. Furthermore, PI3K/AKT/mTOR signalling germline abnormalities can result in inherited diseases linked to a precarious risk of cancer (Polivka *et al*., 2013). In the treatment for ER+/HER2- metastatic breast cancer, everolimus emerged as the initial FDA-approved mTOR inhibitor, targeting

the PI3K/AKT/mTOR cascade to prevent relapse even after hormonal therapy and restore hormonal sensitivity (Baselga *et al.*, 2011; Rodriguez *et al.*, 2023).

Mitogen Activated Protein Kinase- MAPK Pathway

The MAPK pathway, or the mitogen-activated protein kinase pathway, is a signalling pathway that serves as a regulatory network that transmits, amplifies, and processes different extracellular stimuli and converts them into intracellular responses (Zhang *et al.*, 2023). In mammalian systems, this pathway orchestrates basic physiological processes including cellular proliferation, maturation, development, inflammation, and programmed cell death (apoptosis) (Zhang *et al.*, 2023). This MAPK/ERK pathway is crucial to the development, survival, and further growth of the neoplastic cells. The often-targeted signalling pathway by multi-kinase inhibitors is the Mitogen-Activated Protein Kinase (MAPK) cascade, which comprises the RAS–RAF–MEK–ERK signalling segment (Bahar *et al.*, 2023). Three groups of evolutionarily conserved MAPK have been well-defined in mammalian cells: p38 kinase, C-Jun N-terminal kinase/stress-activated protein kinase (JNK/SAPK), and basic MAPK (also called ERK) (Zhang *et al.*, 2023). Any DNA alteration or genomic variation leading to dysregulation or disruption of any MAPK pathway component induces uncontrolled cell growth and tumor development. Targeting with accurate inhibitors in the MAPK pathway can control and cease cell differentiation and tumor progression. The MAPK/RAS/RAF signaling pathway plays an important role in breast cancer, with RAS activation inducing tumor cell proliferation and its further differentiation and among different RAF variants, B-Raf is a vital kinase linked to breast tumorigenesis (Khojasteh *et al.*, 2021). Drugs administered into the body are injected to slow down the growth rate of the tumor and prevent its further progression. Common breast cancer drugs like Sorafenib, Vemurafenib, and Dabrafenib, which are BRAF inhibitors, Ulixertinib, which is an ERK inhibitor, and Farnesyltransferase inhibitors work by targeting the MAPK pathway and block RAS activation, thus disrupting the key signals that induce, initiate, and drive tumor progression (Khojasteh *et al.*, 2021). Simvastatin inhibits both PI3K/Akt/mTOR and MAPK/ERK signaling circuits in BC by dephosphorylating the c-Raf, MEK1/2, and ERK1/2 proteins (Khojasteh *et al.*, 2021).

Hormone Receptor Pathways

Estrogen Receptor (ER), Progestrone Receptor (PR), and Androgen Receptor (AR) pathways fuse into an interplay and comprise an endocrine system that controls cellular growth, proliferation, and further differentiation, dysregulation of which initiates oncogenesis. In hormone-responsive cancers such as prostate, breast and ovarian cancer, androgens and estrogens play a crucial role and have thereby contributed in several deaths (Yap *et al.*, 2021; Brown *et al.*, 2019). Thus, majority of therapeutics in hormone-responsive cancers target specifically androgens and estrogens. Endocrine therapy or hormonal therapy is a vital cornerstone treatment for ER/PR-positive breast cancers that are malignant and androgen-sensitive prostate cancers, which provides sustained outcomes, prolonged survival, and manageable side effects (Boye *et al.*, 2024). Therapies administered in ER/PR-positive breast cancers include adjuvant and neoadjuvant classification of therapies. Adjuvant surgeries are recommended postoperatively to prevent its recurrence in the later stages and remove any remaining cancer cells from the distant anatomical sites of the body, whereas the neoadjuvant surgeries primarily aim to reduce the size of the tumor, making it easier to be removed from the body during surgery. The generation of antiestrogenic medications like tamoxifen which is a Selective Estrogen Receptor Modulator (SERMs) and nafoxidine is the most efficacious new hormonal therapy for estrogen-receptive metastatic breast cancers (Abraham *et al.*, 2022). Patients with advanced metastatic breast cancers are recommended to undergo adrenalectomy in case if the cancer has spread to the adrenal glands and hysterectomy, the removal of the uterus in women considered at higher risk of recurrence and to prevent future occurrence of uterine cancer as a side effect of breast cancer treatment. For postmenopausal women with hormone receptor-positive breast cancer that has spread locally or metastasized, the aromatase inhibitors letrozole and anastrozole are authorized for use as first-line therapies (Legha *et al.*, 1978; Cuzick *et al.*, 2010). Women with more advanced breast cancers are treated with hormonal therapy combined with other targeted therapies. For instance, Abemaciclib (Verzenio), a CDK4/6 inhibitor, is approved along with fulvestrant for postmenopausal women with HR-positive, HER2-negative metastatic breast cancer that has met an advanced stage even after the endocrine or hormonal therapy (Mouridsen *et al.*, 2003).

The Repair Machinery-DNA Damage Response

Morphological changes in the DNA, either endogenous (Replication stress, oxidation, or mismatch of DNA bases) or exogenous (chemicals or chemical radiation), can adversely affect its functions, leading to multiple diseases and cancer. Suppose the DNA is severely damaged and beyond repair. In that case, it can lead to cell cycle arrest and Apoptosis (programmed cell death) (Sledge *et al.*, 2017). Several checkpoints function as a vital component of the DDR pathway. Numerous enzymes that alter DNA and prevent nuclear damage initiate the DNA repair process. Polymerases, topoisomerases, ligases, kinases, phosphatases, and glycosylases comprise the enzymes that assist in repair (Mirza-Aghazadeh-Attari *et al.*, 2018; Ciccia *et al.*, 2010). DDR is activated in dysplastic lesions and acts as a tumor-suppressing pathway, preventing malignant progression (Figure 2). Any mutation or structural changes in the DDR mechanism can lead to genomic instability, initiating the development of a tumor (George *et al.*, 2016).

During DNA replication and transcription, misaligned base pairs, along with tautomeric shifts, lead to incorrectly matched

base pairs. Endogenous factors such as DNA replication and transcription, and exogenous factors such as UV, ionizing radiation, chemical mutagens, and Reactive Oxygen Species (ROS) induce DNA adducts, disrupting repair pathways such as Mismatch Repair (MMR) and Double-Strand Break (DSB) repair. Failure to repair the DNA strands contributes to the mutational burden.

Ionizing radiation promotes its anti-cancer effect and causes breaks in the Double Strands of DNA (DSBs), thus inducing genomic instability, apoptotic signalling, and checkpoint failure in tumor cells (Jiang *et al.*, 2020). It has been studied and reported that three differently functioning basic cascades evolved to process DSB repair: the HR-based pathway (Homologous Recombination), NHEJ (Non-Homologous End Joining), and alternative end joining (Huang *et al.*, 2020). Several Types of DNA damage can be corrected through multiple repair mechanisms, including the excision repair systems: Mismatch Repair (MMR), Base Excision Repair (BER), and Nucleotide Excision Repair (NER) (Huang *et al.*, 2020). Certain targeted therapies include the common PARP group of enzymes that actively participate in cell death. Employing PARP inhibitors is used in the treatment of BRCA1/2-mutated tumors, repairing SSBs (Single-strand breaks) and DSBs that exhibit poorly-repaired DNA repair mechanisms (Gavande *et al.*, 2016). In TP53 oncogene mutated cancers, Ataxia Telangiectasia and Rad-3 inhibitors (ATR) such as Ceralasertib, an oral kinase, target replication stress and function as a novel anti-tumor agent (Lai *et al.*, 2022).

Overview of the Clinically Approved Drugs for Breast Cancer

There are various clinical drugs in the market and this review gives a detailed information about them. The drugs approved by NCI and FDA for treatment of breast cancer are given below Table 1.

The discovery and implications of targeted therapeutics have transformed the treatment paradigms in breast cancer and provided more accurate patient reported outcomes as compared to traditional types of therapies such as chemotherapy. Since the groundbreaking clinical trials from the late 1990s molecular targeted therapies have been designed to disrupt the signalling pathways and have demonstrated incredible efficacy in different subtypes of cancer. These therapies are now the base of precision oncology offering targeted therapeutic treatments (Min *et al.*, 2022).

Novel Therapeutic Approaches

Breast cancer is significantly characterised by signature biomarkers that indicate and drive cellular growth, differentiation, proliferation and progression. Various therapies can inhibit growth factor receptors and diminish proliferative signaling, resulting in apoptosis or other forms of cell death (Seoane *et al.*, 2017; Tokizaki *et al.*, 2024; Xelwa *et al.*, 2021; Tigu *et al.*, 2024). Therapeutic frontiers in have proved out be a cornerstone advancement in the treatment of breast cancer. The development of antibody-drug conjugates has been

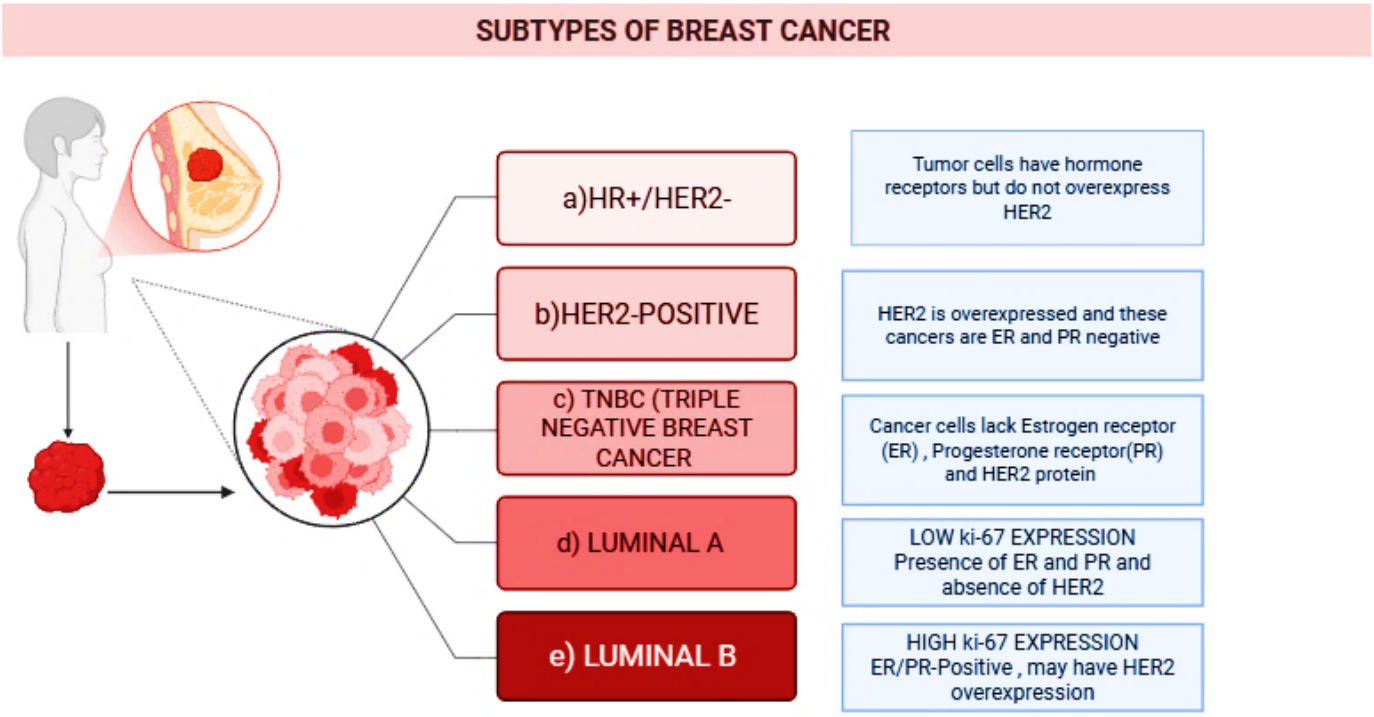

Figure 1: Classification of breast cancer into major molecular subtypes based on hormone receptor (ER/PR) & HER2 expression. These subtypes reflect distinct biological behaviors & guide prognosis & targeted therapeutic strategies (Inic *et al.*, 2014).

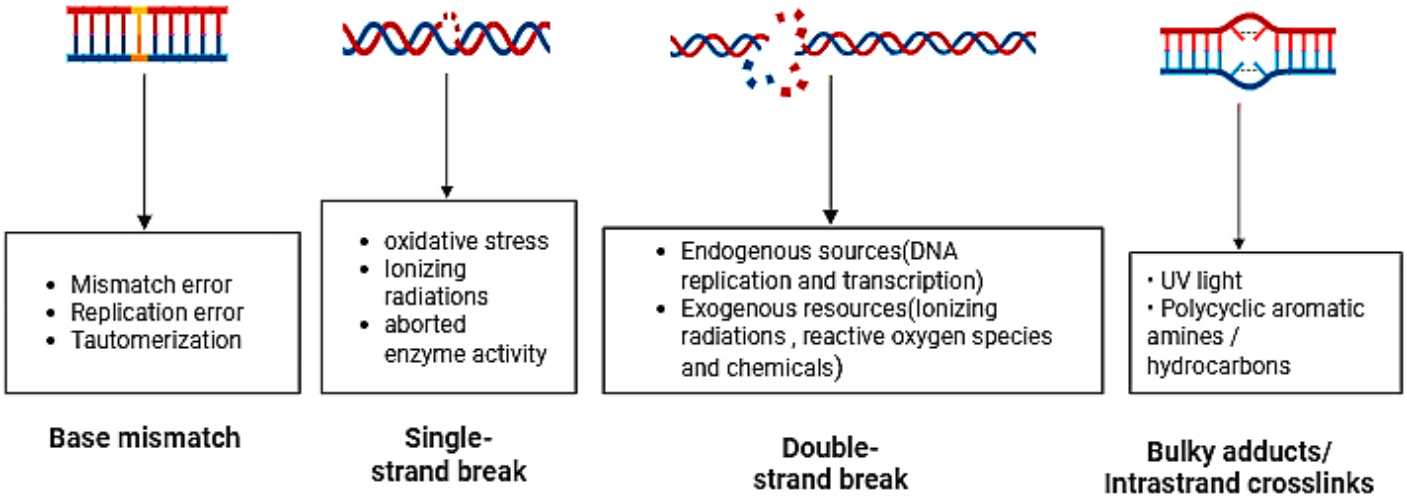

Figure 2: Causes of DNA Damage in the DNA Damage Repair pathway (DDR).

revolutionizing the world around breast cancer. For instance, Sacituzumab Govitecan (Trodelvy) an antibody-drug conjugate that targets metastatic triple negative breast cancer (Bardia *et al.*, 2021). The release of cytotoxic drugs is directly now done into the targeted tumor reign with the help of Antibody-Drug Conjugates (ADCs) allowing for manageable drug toxicity and better patient-reported outcomes (Sun *et al.*, 2024). Immunotherapy as a targeted therapeutic has already been utilized in the treatment of breast cancer and the approval of pembrolizumab by the Food and Drug Administration in combination with chemotherapy in the neoadjuvant and advanced settings of Triple-Negative Breast Cancer (TNBC) has paved the path for the future research and amalgamation of immunomodulatory checkpoint inhibitors in other subfamilies breast cancer (Dvir *et al.*, 2024). Alteration either in the signalling pathways or in the cancer cells are a signature trait of oncogenesis and subsequent altering of the metabolism of glucose, lipids, and amino acids, allow tumor cells to adapt to their surroundings, promoting fast development and treatment resistance (Liu *et al.*, 2024). The further innovative discovery of molecular glues, small monovalent molecules that facilitate protein-protein interaction in a cell leading to protein degradation have been considered a considerable therapeutic innovative to treat breast cancer. For instance, EGFR still remains a challenging protein to be targeted in the triple negative breast cancer (Wang *et al.*, 2025). For the degradation of such proteins like EGFR molecular glues are utilized. Interactions are facilitated between a protein and E3 -ubiquitin ligase thus leading to degradation or removal of such proteins (Wang *et al.*, 2025). Such Protein-Protein Interaction (PPI) interconnections are essential for biological processes such as, homeostatic regulation, cellular proliferation, and differentiation (Konstantinidou *et al.*, 2024).

Combination Therapies as An Emerging Frontier

Combination therapies have become a cornerstone achievement in the reign of breast cancer improving outcomes by targeting multiple pathways at one time and simultaneously reducing the side effects and enhancing the efficacy of the treatments. Combination therapies comprise of basic therapies such as chemotherapy amalgamated with hormonal or immunomodulated. Some of the most utilised combination therapies as listed by the National Cancer Institute (NCI) are CAF (Chemotherapy regimen, definition), CMF (Chemotherapy regimen), FEC (Chemotherapy regimen, definition) and integration of several different therapies in adjuvant or neoadjuvant phases of breast cancer (FDA. 2025; NCI.2025) (Tables 1 and 2). These therapies are said to provide a synergistic effect, for instance trastuzumab + chemotherapy in HER2+ breast cancer (FDA. 2025; NCI.2025; Swain *et al.*, 2015).

Immunotherapies

Recent advances in immunomodulated therapies have revolutionized the already existing immune therapies for breast cancer. For instance, Chemotherapy and cancer immunotherapy based on PD-1 (Programmed cell death protein 1)/PD-L1 (Programmed death-ligand 1) immune checkpoint inhibitors were effective in phase 3 clinical studies for triple-negative breast cancer in both progressed and at early stages (Debien *et al.*, 2023). Another immune based therapy that sparked excitement was the CAR-T cell therapy. Chimeric antigen receptor (CAR) T cell therapy has emerged as a novel therapeutic T cell engineering process, in which T cells derived from patient's blood are engineered in laboratory to express artificial receptors targeted to a specific tumor antigen that attacks body's cancer cells more effectively (Mohanty *et al.*, 2019). These do not rely on the major histocompatibility complex to recognize the tumor antigen (Mohanty *et al.*, 2019). Also, Immune checkpoint inhibitors provide an innovative therapeutic approach for breast cancer and are subject to ongoing research and enhancement (Li *et al.*, 2021; Schmidt *et al.*, 2021; Lau *et al.*, 2022).

Thus, more effective therapeutic mechanisms are being developed to reduce the toxicity caused by basic radiation and

Table 1: Clinically Approved Drugs (2016-2025) from the Database of National Cancer Institute and U.S. Food and Drug Administration (Drugs Approved for Breast Cancer-NCI. 2025; FDA-Approved Drugs, 2025).

Drug Name	Drug Class	Approval Status	Source	Cancer Type	References
Datopotamab Deruxtecan-dlnk (Datroway)	Antibody-drug conjugate	Approved (2025)	NCI, FDA	HR+/HER2-	(FDA. 2025; NCI.2025)
Abemacicilib (verzenio)	CDK4/CDK6 inhibitor	Approved (2017)	NCI, FDA	HR+/HER2-	(FDA. 2025; NCI.2025)
Alpelisib (Piqray Vijoice	Enzyme inhibitor	Approved (2019)	NCI, FDA	HER2-/ mutated PIK3CA	(FDA. 2025; NCI.2025)
Fam trastuzumab deruxtecan-nxki (Enhertu)	Antibody-drug conjugate	Approved (2025)	NCI, FDA	HER2-positive	(FDA. 2025; NCI.2025
Sacituzumab Govitecan (Trodelvy)	Anti-body-drug conjugate	Approved (2021)	NCI, FDA	mTNBC	(FDA. 2025; NCI.2025)
Inavolisib (Itovebi)	Enzyme Inhibitor	Approved (2024)	NCI, FDA	HER2-/Abnormal PIK3CA	(FDA. 2025; Bardia et a., 2021)
Ado-Trastuzumab Emtansine (Kadcyla)	Antibody-drug conjugate	Approved (2019)	NCI	HER2+	(FDA. 2025; Wedam *et al.*, 2020)
Talazoparib Tosylate (Talzenna)	PARP inhibitor	Approved (2018)	NCI, FDA	HER2-/BRCA Mutated	(FDA. 2025; NCI.2025)
Palbociclib (Ibrance)	CDK4/6 Inhibitor	Approved (2016)	NCI, FDA	HR+/HER2-	(FDA. 2025; NCI.2025).
Pembrolizumab (Keytruda)	Immune checkpoint inhibitor	Approved (2021)	NCI, FDA	TNBC	(FDA. 2025; NCI.2025).

chemotherapies and enhance efficacy by providing more precise and targeted therapeutics.

Future Prospectives

Advancements have shaped our understanding of the underlying molecular mechanisms in breast cancer. Techniques such as liquid biopsies, non-invasive method for detecting and assessing tumors in the absence of tissue samples (Angeles *et al.*, 2021). and genome profiling provide an in-depth insight into the early and later stages of tumor development. Precision medicine is the new era of targeted therapy providing a more holistic approach and better patient reported outcomes. The NCI has also initiated a clinical experiment titled NCI-Match, wherein patients receive medication based on the genetic mutations diagnosed in their tumors rather than at the precise spot of the disease (NC Institute, 2021; Sauter *et al.*, 2018). Integration of AI based diagnosis and Targeting multiple signaling pathways with an individual personalized drug could also accelerate the screening and monitoring at an early stage of breast cancer. To facilitate the identification of new biomarkers for breast cancer single cell technologies are highly elucidated providing an in-depth insight (Hong *et al.*, 2022). For instance, a single-cell research analysis indicated that the plethora of the CXCL13-positive T cell subfamily predicted responses to anti-PD-L1 therapy in Triple-Negative Breast Cancer (TNBC) (Zhang *et al.*, 2021; Hong *et al.*, 2022). Thus, AI based models, precision oncology and immunomodulated therapies are the futuristic approaches to provide therapeutics that eliminates toxicity and provides a more prolonged survival.

Future Directions

Recent progress in breast cancer treatment focuses on targeting tumors more precisely by better understanding molecular pathways & creating new therapies. Because breast cancer is so varied, improved molecular profiling helps classify subtypes more accurately, which supports more personalized care. Researchers are now developing targeted treatments that go beyond hormone receptors and HER2. They are studying the PI3K/AKT/mTOR, MAPK, & DNA repair pathways to develop new inhibitors, combination treatments, and ways to overcome resistance. These

Table 2: Highlighting the breast cancer subtypes and the type of combination therapy used against them with reduced side effects and enhanced efficacy.

Bc Subtype	Combination Therapies	Drugs Used	References
HER2-Positive	Targeted therapy+chemotherapy	Trastuzumab+Pertuzumab +Docetaxel	(Swain *et al.*, 2015)
HR+ (Human Receptor Positive)/HER2-	1.Hormone Therapy+CDK4/6 Inhibitor 2.mTOR inhibitor+ Aromatase inhibitor	1.Letrozole+palbociclib 2.Everolimus+ Exemestane	(O'Shaughnessy *et al.*, 2018)
TNBC	Chemotherapy+ immunotherapy	Pembrolizumab + Paclitaxel/ Carboplatin	(Schmid *et al.*, 2020)

efforts aim to make treatments last longer and lower the chances of relapse. Immunotherapy is also a key area, especially immune checkpoint inhibitors, which show promise for triple-negative breast cancer. Current studies are working to identify predictive biomarkers, improve combination therapies, & alter the tumor microenvironment to boost immune responses. New methods, such as epigenetic targeting and RNA-based therapies, are being tested to control gene expression and address resistance. Researchers are also improving antibody-drug conjugates & nanotechnology-based delivery systems to target tumors more specifically and reduce side effects.

Bringing together artificial intelligence, liquid biopsies, and real-time molecular monitoring is expected to change how doctors make decisions in breast cancer care. These tools should help spot resistance to treatment early and allow for quick changes to therapy, moving the field closer to true precision medicine.

CONCLUSION

Breast cancer causes death worldwide and remarkable advancements has been made in this field. This review discussed multiple signaling pathways and the targeted therapies such as immunotherapies, PARP inhibitors, Antibody-Drug Conjugates (ADCS) and enzyme inhibitors. These innovations have significantly improved yet more personalized approach is the need of the hour. The precision and the targeted therapies discussed in the review can change the view of the onlookers and patients suffering from breast cancer who are still struggling to find a cure and avoid its recurrence in the later stages.

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ABBREVIATIONS

BC: Breast cancer; **HR+:** Human Receptor Positive; **HER 2:** Human epidermal growth factor two; **IHC:** Immunohistochemistry; **ER:** Estrogen-Receptor; **FISH:** Fluorescence *in situ* hybridisation; **FEC:** Chemotherapy regimen; definition; **TNBC:** Triple negative Breast cancer; **EGFR:** Epidermal Growth Factor Receptor; **TKIs:** Tyrosine kinase inhibitors; **T-DM1:** Trastuzumab Emtansine; **T-DXd:** Trastuzumab deruxtecan; **PD-1:** Programmed cell death protein 1; **PD-L1:** Programmed death-ligand 1; **PI3K:** Phosphatidylinositol 3-kinase; **Mtor:** Mammalian target of rapamycin; **MAPK:** Mitogen-activated protein kinase; **PR:** Progesterone receptor; **AR:** Androgen receptor; **SERMs:** Selective estrogen receptor modulator; **SSBs:** Single-strand breaks; **ROS:** Reactive oxygen species; **MMR:** Mismatch repair; **DSB:** Double-strand break; **HR:** Homologous Recombination; **NHEJ:** Non-Homologous End Joining; **BER:** Excision repair; **NER:** Nucleotide excision repair; **ADCs:** Antibody-drug conjugates; **TNBC:** Triple-negative breast cancer; **PPI:** Protein-protein interaction; **NCI:** National Cancer Institute; **CAR:** Chimeric antigen receptor; **CAF:** Chemotherapy regimen, definition; **CMF:** Chemotherapy regimen.

AUTHOR CONTRIBUTIONS

Mohammed Tarique designed and supervised the study and drafted the manuscript. Abdulmajeed Sindi collected the data and reviewed the literature. Nawal Helmi revised the manuscript. Qamre Alam conducted the final review. All authors approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no challenging interests

GENERATIVE AI STATEMENT

The author declares that Generative AI (Artificial Intelligence) tools, including, Grammarly, and QuillBot, was used to enhance the language & clarity of this work. I take full responsibility for the accuracy & integrity of the content.

SUMMARY

Breast cancer is one of the most common cancers in women and remains a leading cause of death worldwide. Molecular markers like ER/PR, HER2, & Ki-67 help classify subtypes, guide diagnosis, & advise treatment. Other biomarkers also play a role in personalizing therapy. This review covers key signaling pathways, recent advances in precision oncology, & new targeted or combination therapies.

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