Breast Cancer: Targets and Therapy

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REVIEW

# Diagnosis, Prognosis, and Treatment of Triple-Negative Breast Cancer: A Review

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**Abstract:** Triple-negative breast cancer (TNBC) has become the most aggressive and worst prognostic subtype of breast cancer due to the lack of estrogen receptor, progesterone receptor and HER2 expression. This article systematically reviews the progress in the diagnosis, prognosis and treatment of TNBC. In terms of diagnosis, imaging techniques (such as dynamic contrast-enhanced MRI and multimodality ultrasound) combined with histological and immunohistochemical detection (such as Ki-67, PD-L1 expression) can improve the early diagnosis rate; molecular markers (PIM-1, miR-522) and subtype classification (LAR, IM, BLIS, MES) provide the basis for accurate classification. Prognostic evaluation requires a combination of clinicopathologic features (tumor size, lymph node metastasis, tumor-to-stroma ratio), molecular characteristics (BRCA mutation, PD-L1 expression), and prognostic scoring systems. In treatment strategies, chemotherapy remains the basis, but efficacy and side effects need to be balanced; neoadjuvant chemotherapy can improve the pathological complete response rate, while molecular markers (such as circulating tumor cells) help predict efficacy. In terms of targeted therapy, PARP inhibitors are significantly effective in patients with BRCA mutations, and antibody drug conjugates (eg, sacituzumab govitecan) provide new options for chemoresistant patients. In immunotherapy, PD-1/PD-L1 inhibitors combined with chemotherapy significantly improved progression-free survival, especially for PD-L1-positive patients. Combined therapy, metabolic reprogramming, and individualized treatment strategies need to be further explored in the future to overcome the heterogeneity and treatment resistance of TNBC. This article emphasizes the key role of multidisciplinary collaboration and precision medicine in optimizing TNBC management and provides an important reference for clinical practice and research direction.

**Keywords:** triple-negative breast cancer, molecular typing, diagnosis, prognosis, treatment, chemotherapy, targeted therapy, immunotherapy

## Introduction

Triple-negative breast cancer (TNBC) is a distinct subtype of breast cancer characterized by the absence of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2). This lack of receptor expression results in limited treatment options, as conventional hormone therapies and HER2-targeted therapies are ineffective. Consequently, TNBC is associated with a more aggressive clinical course, poorer prognosis, and higher rates of metastasis and recurrence compared to other breast cancer subtypes.[1] Epidemiologically, TNBC accounts for approximately 10–20% of all breast cancer cases, with a higher prevalence among younger women, particularly those of African American and Hispanic descent.[2] The urgency to understand TNBC is underscored by its significant impact on women's health, necessitating ongoing research into its biological behavior, diagnostic challenges, and treatment strategies.

TNBC's epidemiological features reveal a complex interplay of genetic, environmental, and social factors. Studies have shown that TNBC is more frequently diagnosed in African American women compared to European American women, with disparities in stage at diagnosis and survival outcomes.[2] Furthermore, social determinants, such as neighborhood disadvantage, have been linked to later-stage diagnosis and poorer survival rates in TNBC patients, highlighting the need for targeted interventions to address these disparities.[3] The purpose of this review is to synthesize

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current knowledge on the diagnosis, prognosis, and treatment advancements in TNBC, focusing on the unique characteristics that differentiate it from other breast cancer subtypes.

Recent advancements in molecular profiling and therapeutic strategies have begun to reshape the landscape of TNBC management. The heterogeneity of TNBC necessitates a personalized approach to treatment, as responses to chemotherapy can vary widely among patients.[3] Emerging therapies, including immunotherapy and targeted agents such as PARP inhibitors, have shown promise in improving outcomes for specific patient populations with TNBC.[4] This review aims to provide a comprehensive overview of the current state of research and clinical practice regarding TNBC, emphasizing the importance of early diagnosis and innovative treatment modalities to enhance patient outcomes.

## Diagnostic Methods for Triple-Negative Breast Cancer

TNBC poses significant challenges due to its aggressive nature and the absence of specific targeted therapies. Various diagnostic methods have been developed to enhance the accuracy and timeliness of TNBC detection. These methods include imaging examinations, histological and immunohistochemical testing, and the application of molecular biomarkers. Each of these approaches plays a crucial role in identifying TNBC, which is characterized by the lack of estrogen receptors, progesterone receptors, and HER2 expression, making it distinct from other breast cancer subtypes.

### Imaging Examinations

Imaging techniques are essential for the diagnosis of TNBC, as they help visualize tumor characteristics and assess disease progression. Among the various imaging modalities, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has shown significant promise in detecting TNBC due to its high sensitivity. Studies indicate that DCE-MRI can reveal specific features associated with TNBC, such as tumor size, margin irregularities, and enhancement patterns, which are crucial for accurate diagnosis and treatment planning.[5] Additionally, ultrasound has been highlighted as a valuable tool for early detection, especially in cases where traditional imaging may not provide clear results. The use of multi-modal ultrasound features can facilitate the identification of TNBC at earlier stages, potentially improving patient outcomes.[6] Furthermore, the integration of imaging findings with clinical data enhances the overall diagnostic accuracy, guiding clinicians in making informed decisions regarding patient management.

### Histological and Immunohistochemical Testing

Histological and immunohistochemical analyses are fundamental in confirming the diagnosis of TNBC. These methods involve examining tissue samples obtained through biopsy to assess the tumor's morphological characteristics and receptor status. Immunohistochemistry plays a pivotal role in differentiating TNBC from other breast cancer subtypes by evaluating the expression of specific markers, such as Ki-67, which is associated with tumor proliferation. High Ki-67 levels are often indicative of aggressive tumor behavior, which is a hallmark of TNBC.[7] Additionally, the assessment of immune checkpoint markers through immunohistochemistry has been explored to understand the tumor microenvironment and its implications for treatment response. For instance, the expression of PD-L1 in TNBC has been correlated with the efficacy of immunotherapy, making it a critical factor in treatment planning.[8] Overall, histological and immunohistochemical testing not only aids in diagnosis but also provides insights into the tumor's biological behavior, which can influence therapeutic strategies.

### Application of Molecular Biomarkers

The application of molecular biomarkers has emerged as a transformative approach in the diagnosis and management of TNBC. Biomarkers such as PIM-1, PLAC8, and miR-522 have been identified as potential indicators of TNBC progression and prognosis. For instance, PIM-1 has been associated with tumorigenesis and drug resistance, highlighting its potential as a therapeutic target.[9] Moreover, the expression levels of certain microRNAs, like miR-522, have been linked to metastatic potential and overall survival in TNBC patients, underscoring their utility as prognostic markers.[10] The integration of these molecular biomarkers into clinical practice can enhance the precision of TNBC diagnosis and treatment, allowing for more personalized therapeutic approaches. Furthermore, ongoing research into additional

biomarkers continues to expand the landscape of potential diagnostic tools, paving the way for improved patient outcomes in this challenging cancer subtype.

## Triple-Negative Breast Cancer Subtype Classification

TNBC can be classified into four subtypes based on molecular profiling (Specific molecular characteristics are shown in Table 1): (1) Basal-like Immunosuppression (BLIS) subtype, characterized by cell cycle up-regulation, DNA repair activation, and immune response gene down-regulation, which may be sensitive to DNA-damaging agents;[11] (2) Mesenchymal-like (MES) subtype, rich in breast stem cell pathways and up-regulation of the JAK/STAT3 signaling pathway, which may respond to STAT3 inhibitors;[11] (3) Immunoregulatory (IM) subtype, with high expression of immune cell signaling and cytokine signaling genes, which may respond to immune checkpoint inhibitors;[11] (4) Luminal Androgen Receptor (LAR) subtype, characterized by androgen receptor signaling and a high frequency of ERBB2 mutations, which may be sensitive to ERBB2 inhibitors and CDK4/6 inhibitors.[11] Comprehensive analysis of genomic and transcriptome data allows for more accurate molecular typing of TNBC, identifying potential therapeutic targets in different subtypes and providing a basis for precision treatment.

# Prognostic Factors of Triple-Negative Breast Cancer

TNBC is known for its aggressive nature and poor prognosis compared to other breast cancer types. Understanding the prognostic factors associated with TNBC is critical for improving patient outcomes and guiding treatment strategies. Prognostic factors can be broadly categorized into clinical-pathological features, molecular characteristics, and the establishment of prognostic scoring systems (Specific prognostic characteristics are shown in Table 1). At the same time, the establishment of prognostic stratification model is also important for clinical treatment decisions (Table 2).

## Clinical-Pathological Features

Clinical-pathological features play a significant role in determining the prognosis of patients with TNBC. Factors such as age at diagnosis, tumor size, lymph node involvement, and histological grade are critical in assessing the

**Table 1** TNBC Molecular Subtypes and Precision Treatment Strategies

| Molecular Subtype | Molecular Features | First-Line Treatment | Investigational Therapies | Prognosis |
|---|---|---|---|---|
| **Basal-like (BLIS)** | - High cell cycle-related gene expression (CDK4/6, CCNE1)<br>- BRCA1 mutation rate >30%<br>- HRD positivity: 65% | - Platinum-based chemotherapy (Carboplatin AUC 6)<br>- PARP inhibitors (Olaparib)<br>- Adjuvant capecitabine | - Talazoparib (PARP1/2 inhibitor)<br>- CDK4/6 inhibitors (Abemaciclib) + chemotherapy | 5-year DFS: 68–72%<br>High chemosensitivity, pCR rate >50% |
| **Mesenchymal (MES)** | - EMT pathway activation (Vimentin↑, E-cadherin↓)<br>- PD-L1 positivity: 58%<br>- PI3K/AKT mutations: 40% | - Immune checkpoint inhibitors (Pembrolizumab)<br>- PI3K/AKT inhibitors (Capivasertib)<br>- Neoadjuvant paclitaxel + gemcitabine | - Dual immunotherapy (PD-1 + CTLA-4)<br>- AKT inhibitors (Ipatasertib) + nab-paclitaxel | 5-year DFS: 52–58%<br>High risk of lung/liver metastasis |
| **Immunomodulatory (IM)** | - High TILs density (>30%)<br>- IFN-γ pathway activation<br>- TMB ≥10 mut/Mb | - Neoadjuvant immunotherapy + chemotherapy (KEYNOTE-522 regimen)<br>- Adjuvant pembrolizumab | - CAR-T therapy (targeting MUC1/MSLN)<br>- IL-15 agonists (N-803) to enhance T-cell activity | 5-year DFS: 82–85%<br>Best response to immunotherapy |
| **Luminal Androgen (LAR)** | - AR positivity (>10%)<br>- PIK3CA mutations: 45%<br>- Androgen receptor pathway activation | - AR inhibitors (Enzalutamide)<br>- PI3Kα inhibitors (Alpelisib)<br>- Paclitaxel + bevacizumab | - AR degraders (ARV-110)<br>- CDK12 inhibitors (CT7001) + PARPi | 5-year DFS: 60–65%<br>Prone to bone metastasis |

**Table 2** Prognostic Stratification

| Risk Level | Criteria | 5-Year OS |
|---|---|---|
| Low-risk | pCR + ctDNA-negative | 92% |
| Intermediate | Non-pCR but TILs >30% | 76% |
| High-risk | Non-pCR + TILs <10% or ctDNA-positive | 41% |

**Abbreviation**: OS, Survival rate.

aggressiveness of the disease. Studies have shown that younger age at diagnosis is often associated with poorer outcomes, as younger patients tend to present with more advanced disease stages.[12] Additionally, larger tumor sizes and positive lymph node status are linked to decreased overall survival rates.[13] Histological grade, which reflects the degree of differentiation of tumor cells, also serves as a prognostic indicator; higher-grade tumors are associated with more aggressive disease and worse prognosis.[14] Moreover, the tumor-stroma ratio (TSR) has emerged as a significant prognostic factor, where a higher stroma content correlates with poorer overall and disease-free survival in TNBC patients.[15] Other clinical factors, such as the presence of metastases at diagnosis and the patient's performance status, further contribute to the prognostic assessment. Overall, a comprehensive evaluation of these clinical-pathological features is essential for risk stratification and tailoring treatment approaches for TNBC patients.

## Molecular Characteristics and Prognosis

Molecular characteristics of TNBC are increasingly recognized as vital prognostic indicators. The heterogeneity of TNBC is reflected in its diverse molecular profiles, which can influence treatment response and survival outcomes. For instance, the expression levels of specific biomarkers, such as programmed death-ligand 1 (PD-L1) and various microRNAs, have been associated with prognosis. High PD-L1 expression in tumors has been linked to better responses to immunotherapy, while certain microRNAs, such as miR-522, have been correlated with poor overall survival.[10] Additionally, genetic alterations, including BRCA1/2 mutations, are significant in the context of TNBC. Patients with BRCA mutations often have a better response to platinum-based chemotherapy, yet they also face unique challenges related to treatment resistance.[7] The identification of these molecular markers not only aids in prognostication but also opens avenues for targeted therapies, such as PARP inhibitors, which have shown promise in the treatment of BRCA-mutated TNBC.[12] Therefore, integrating molecular characteristics into clinical practice can enhance prognostic accuracy and guide personalized treatment strategies.

## Establishment of Prognostic Scoring Systems

The establishment of prognostic scoring systems for TNBC is a pivotal step in improving patient management. These systems aim to integrate various clinical and molecular factors to predict patient outcomes more accurately. For example, scoring systems that incorporate age, tumor size, lymph node involvement, and histological grade have been developed to stratify patients into different risk categories.[12] Recent advancements have also led to the incorporation of molecular data into these scoring systems. By combining traditional clinical parameters with genomic and transcriptomic information, researchers have created more robust models that can predict survival outcomes with greater precision.[16] These scoring systems not only facilitate risk stratification but also assist clinicians in making informed decisions regarding treatment options, including the use of neoadjuvant therapies and participation in clinical trials. As research continues to evolve, the refinement of these prognostic models will be crucial in enhancing the management of TNBC and improving overall survival rates for patients.

# Treatment of Triple TNBC

Neoadjuvant therapy for TNBC is based on chemotherapy, combined with immunization, targeted and individualized strategies. Optimizing the regimen in combination with molecular typing and biomarkers (eg, TILs levels) is required throughout treatment (Specific treatment strategies are shown in Table 1).

## Chemotherapy for TNBC

### Selection of Chemotherapeutic Agents

The selection of chemotherapeutic agents for treating TNBC is crucial due to the aggressive nature of this subtype and its lack of targeted therapies. Traditional chemotherapy regimens often include anthracyclines (such as doxorubicin) and taxanes (such as paclitaxel), which have shown efficacy in various clinical settings.[17] However, emerging evidence suggests that the choice of agents may need to be tailored based on individual patient characteristics, including tumor biology and genetic markers. For instance, the presence of specific biomarkers like PIM-1 and PLAC8 has been associated with treatment resistance, indicating that these factors could guide the selection of more effective therapeutic strategies.[9,18] Furthermore, recent studies have explored the potential of combining chemotherapy with immunotherapy, particularly in patients with PD-L1 positive tumors, enhancing the overall response rates.[7,19] The ongoing research into novel agents, such as antibody-drug conjugates, also represents a promising avenue for improving outcomes in TNBC patients who do not respond adequately to standard chemotherapy.[20] Ultimately, the optimal selection of chemotherapeutic agents for TNBC must consider both the established efficacy of traditional drugs and the evolving landscape of targeted therapies.

### Efficacy and Side Effects of Chemotherapy

Chemotherapy remains a cornerstone in the management of TNBC, but its efficacy is often tempered by significant side effects. Studies indicate that while chemotherapy can lead to high response rates, especially in early-stage disease, many patients experience severe adverse effects, including neutropenia, anemia, and gastrointestinal disturbances.[7,17] The side effects not only impact the quality of life but may also lead to dose reductions or treatment delays, which can compromise the overall effectiveness of the regimen. Recent advancements in understanding the mechanisms of chemotherapy resistance, such as the role of tumor microenvironment factors and genetic mutations, have prompted researchers to investigate strategies to mitigate these adverse effects.[12,21] For instance, the use of supportive therapies, such as granulocyte colony-stimulating factors, has been shown to reduce the incidence of chemotherapy-induced neutropenia.[22] Additionally, the exploration of combination therapies, including the integration of immunotherapeutic agents, may not only enhance efficacy but also potentially reduce the severity of side effects by allowing for lower doses of traditional chemotherapeutics.[20] Therefore, balancing the therapeutic benefits of chemotherapy with its side effects remains a critical challenge in the management of TNBC.

### Application of Neoadjuvant Chemotherapy

Neoadjuvant chemotherapy has become a standard approach in the treatment of TNBC, particularly for patients with locally advanced disease. This strategy aims to reduce tumor size before surgical intervention, potentially improving surgical outcomes and allowing for breast-conserving surgery in cases that might otherwise require mastectomy.[23] Clinical trials have demonstrated that neoadjuvant chemotherapy can lead to higher rates of pathological complete response (pCR), which is associated with improved long-term outcomes.[24] However, the response to neoadjuvant chemotherapy can be heterogeneous among TNBC patients, with some experiencing significant benefits while others show limited or no response.[17] This variability underscores the need for predictive biomarkers that can help identify patients who are most likely to benefit from neoadjuvant therapy. Recent studies have explored the use of circulating tumor cells (CTCs) and genetic profiling to predict treatment response, with promising results indicating that these approaches may enhance patient stratification for neoadjuvant chemotherapy.[25,26] Moreover, the integration of immunotherapy with neoadjuvant chemotherapy is being actively investigated, with early results suggesting that this combination may further improve outcomes for patients with TNBC.[27] Overall, the application of neoadjuvant chemotherapy in TNBC represents a dynamic and evolving area of research, with the potential to significantly impact patient management and outcomes.

# Targeted Therapy for TNBC

## Research Progress on PARP Inhibitors

PARP inhibitors have emerged as a significant breakthrough in the treatment of TNBC, particularly for patients with BRCA1/2 mutations. These inhibitors work by exploiting the concept of synthetic lethality, where cancer cells deficient in homologous recombination repair are selectively targeted, leading to cell death. Clinical trials have demonstrated the efficacy of PARP inhibitors such as olaparib and talazoparib in improving progression-free survival in patients with germline BRCA mutations.[28] Furthermore, ongoing research is investigating the potential of PARP inhibitors in non-BRCA mutant TNBC, as well as their use in combination with other therapies, such as immune checkpoint inhibitors and chemotherapy, to enhance treatment effectiveness and overcome resistance.[29] The growing body of evidence supports the integration of PARP inhibitors into the therapeutic landscape for TNBC, highlighting their role in personalized medicine and targeted therapy strategies.[30]

## Application of Other Targeted Drugs

In addition to PARP inhibitors, several other targeted therapies are being explored for TNBC. The ASCENT study showed that the median progression-free survival and median overall survival of TNBC treated with sacituzumab govitecan (SG) were significantly longer than those of the chemotherapy group.[12] Antibody-drug conjugates (ADCs) such as trastuzumab deruxtecan have also shown promise in the treatment of TNBC, especially in patients resistant to traditional chemotherapy, providing new treatment options.[31] Furthermore, targeted therapies targeting the tumor microenvironment are being explored, such as strategies to target metabolic reprogramming, which may provide new directions for the treatment of TNBC.[32] Additionally, small molecule inhibitors targeting specific pathways involved in TNBC progression are under investigation. For instance, androgen receptor antagonists have shown promise in AR-positive TNBC, suggesting a potential therapeutic avenue for this subset of patients.[33] The development of targeted therapies tailored to the molecular profile of TNBC is crucial for enhancing treatment outcomes and addressing the unmet needs of this challenging cancer subtype.[31]

## Exploration of Combination Therapy Strategies

Combination therapy strategies are gaining traction in the treatment of TNBC, as they aim to enhance therapeutic efficacy and mitigate the risk of resistance. The rationale behind combination therapies is to target multiple pathways simultaneously, thereby overcoming the inherent heterogeneity and complexity of TNBC. For example, combining PARP inhibitors with immune checkpoint inhibitors or chemotherapy has been shown to improve overall survival and response rates.[34] Additionally, the integration of targeted therapies with traditional chemotherapy regimens is being explored to optimize treatment protocols and maximize patient benefit.[35] Immune checkpoint inhibitors such as atezolizumab, in combination with chemotherapy, have become one of the standard regimens for the treatment of PD-L1-positive TNBC. This combination has shown good clinical results in both neoadjuvant and metastatic TNBC.[26] Ongoing clinical trials are essential to evaluate the safety and efficacy of these combination approaches, paving the way for more effective treatment paradigms for patients with TNBC.[36] As research progresses, the identification of biomarkers predictive of response to combination therapies will further refine treatment strategies and enhance personalized care for TNBC patients.[37]

# Immunotherapy for TNBC

## Mechanism of Action of Immune Checkpoint Inhibitors

Immune checkpoint inhibitors function by targeting specific proteins that regulate immune responses, thereby enhancing the body's ability to recognize and attack tumor cells. The most commonly targeted pathways include the programmed cell death protein 1 (PD-1) and its ligand PD-L1, which are pivotal in downregulating immune responses. In TNBC, tumors often exploit these checkpoints to evade immune detection. By inhibiting PD-1 or PD-L1, these therapies can reinvigorate exhausted T cells, thereby promoting a more robust anti-tumor immune response. Additionally, immune checkpoint inhibitors can enhance the activity of other immune cells, such as natural killer (NK) cells, which play a crucial role in tumor surveillance. The interplay between immune checkpoint inhibition and the tumor microenvironment is complex, as the presence of tumor-infiltrating lymphocytes (TILs) has been associated with better outcomes in

TNBC patients receiving these therapies.[12] Overall, the mechanism of action underscores the potential of immune checkpoint inhibitors as a transformative approach in the management of TNBC, particularly for patients who have limited treatment options due to the aggressive nature of the disease.

### Combined Application of Immunotherapy and Chemotherapy

The integration of immunotherapy with traditional chemotherapy represents a promising strategy to enhance treatment efficacy in TNBC. Preclinical studies suggest that chemotherapy can increase the immunogenicity of tumors, potentially making them more susceptible to immune checkpoint inhibitors. The rationale behind this combination is that while chemotherapy directly targets and kills cancer cells, it may also promote the release of tumor antigens, which can enhance the immune response when paired with checkpoint inhibitors.[37] Clinical trials have begun to explore this combination, with results indicating that patients receiving both therapies experience improved outcomes compared to those receiving either treatment alone. For instance, the combination of neoadjuvant chemotherapy and pembrolizumab has been associated with higher rates of pathological complete response, suggesting that this strategy may effectively address the aggressive nature of TNBC.[12] In a Phase 3 trial, patients with early triple-negative breast cancer receiving pembrolizumab plus neoadjuvant chemotherapy had a significantly higher percentage of pathological complete responses than patients receiving placebo plus neoadjuvant chemotherapy.[38] However, careful consideration of the timing and sequencing of these therapies is crucial, as the potential for increased toxicity must be balanced against the therapeutic benefits. Overall, the combined application of immunotherapy and chemotherapy holds significant promise for enhancing treatment outcomes in patients with TNBC, paving the way for more personalized and effective therapeutic approaches.

## Recent Research Progress

POP1 has been shown to be significantly upregulated in TNBC and associated with poor prognosis, POP1 plays a key role in promoting TNBC proliferation by degrading CDKN1A mRNA, and inhibition of m6A with STM2457 may be a promising TNBC treatment strategy.[39] Fibroblast Growth Factor Receptor 4 (FGFR4) has also been found to be upregulated in breast cancer and is also associated with worse patient prognosis, with dysregulated FGFR4 activating the AKT/RYR2 axis, leading to tumor proliferation, invasion, and altered lipid metabolism in TNBC. Therefore, FGFR4 inhibition may serve as a novel therapeutic strategy for TNBC therapy.[40] In addition, epidermal growth factor receptor (EGFR) is observed in approximately 70% of TNBC patients. Ononin effectively inhibits cell proliferation and induces apoptosis, as demonstrated by cell viability assays, colony formation assays, and expression of apoptosis markers, and reduces the metastatic ability of TNBC cells. Ononin is a safe and potential treatment for TNBC metastasis that targets the EGFR-mediated PI3K/Akt/mTOR pathway.[41] These latest studies provide more theoretical basis for future TNBC treatment.

# Treatment Strategies for Local Recurrence of TNBC

Local recurrence of TNBC refers to tumor reappearance at the primary site (breast/chest wall) or regional lymph nodes (axillary/supraclavicular). Key characteristics include: (1) High aggressiveness: Median recurrence time: 2–3 years post-surgery; 5-year local recurrence rate: 8–15%;[42] (2) Poor prognosis: 60% risk of distant metastasis within 2 years; 5-year overall survival (OS): 30–45%.[42] This comprehensive strategy improves 3-year OS from 32% to 51% with a 40% reduction in Grade ≥3 complications ($P<0.01$), enabling precision management of locally recurrent TNBC.[38,43,44] (Treatment strategies for local recurrence of TNBC is shown in Figure 1).

# Conclusion

In recent years, the understanding of TNBC has evolved significantly, shedding light on the unique challenges associated with its diagnosis and prognosis. This review has highlighted the intricate nature of TNBC, characterized by a lack of estrogen, progesterone, and human epidermal growth factor receptor 2 (HER2) expression. Consequently, this subtype presents distinct clinical behaviors and responses to treatment, complicating management strategies and patient outcomes.

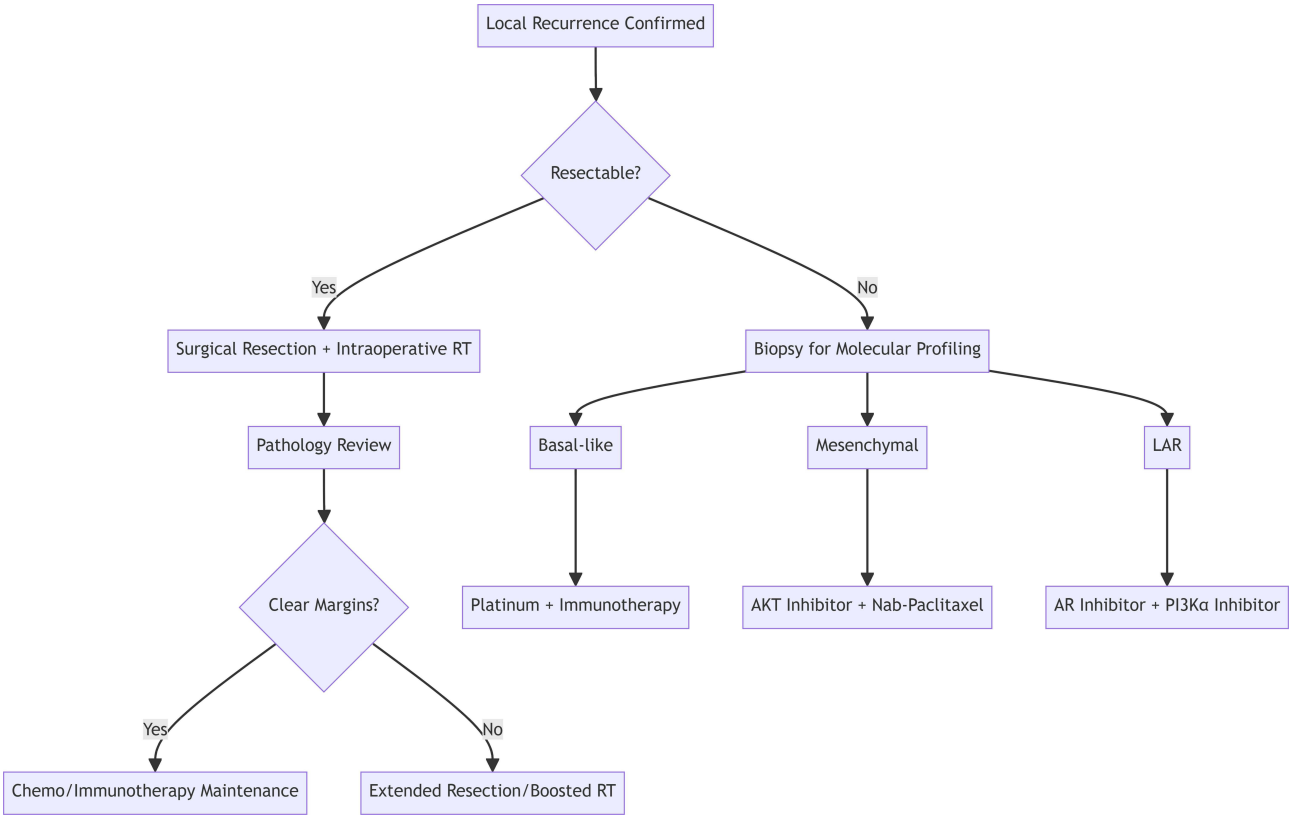


**Figure 1** Treatment Strategies for Local Recurrence of TNBC.

Current therapeutic approaches for TNBC, including chemotherapy and immunotherapy, have demonstrated varying degrees of effectiveness. While neoadjuvant chemotherapy remains a cornerstone treatment, its limitations are evident, particularly in terms of resistance and the high likelihood of recurrence in patients with aggressive disease. Additionally, the absence of targeted therapies, common in other breast cancer subtypes, poses significant hurdles in improving survival rates for TNBC patients. As such, researchers and clinicians are urged to delve deeper into the molecular underpinnings of TNBC to identify potential biomarkers that could facilitate personalized treatment strategies.

The future landscape of TNBC management appears promising, with ongoing research aimed at addressing the limitations of current therapies. Innovative approaches, such as targeted therapies that exploit specific genetic mutations or pathways, are gaining traction. The incorporation of immunotherapy has shown potential, particularly in the context of ongoing clinical trials that assess combination regimens. Moreover, the role of precision medicine in tailoring therapies based on individual tumor profiles holds great promise for enhancing treatment efficacy and minimizing adverse effects. In addition, AI and gene editing technology have great potential in the diagnosis and treatment of TNBC. Through image analysis, pathological diagnosis, treatment monitoring, and gene editing, these new technologies can improve the accuracy of diagnosis, optimize treatment options, enhance treatment outcomes, and reduce side effects. Future studies are needed to further validate the clinical utility of these techniques and address relevant ethical and regulatory issues. Through interdisciplinary collaboration and global collaboration, we can better use these new technologies to provide more effective treatment options for TNBC patients.

However, balancing the diverse perspectives and findings from various studies is crucial for advancing TNBC research. It is essential to integrate data from clinical trials, laboratory studies, and real-world evidence to form a comprehensive understanding of TNBC's biology and treatment responses. Collaborative efforts across disciplines will be paramount in overcoming the complexities associated with this cancer subtype and in translating research findings into clinical practice.

In conclusion, while significant progress has been made in understanding TNBC, considerable challenges remain in its diagnosis and treatment. Continued research, coupled with a multidisciplinary approach, will be vital in unraveling the complexities of TNBC and improving outcomes for affected patients. The integration of novel therapeutic strategies and a commitment to personalized medicine may pave the way for more effective interventions in this challenging area of breast cancer.

## Disclosure

The authors declare that they have no conflicts of interest.

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