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Review Article

AI-based precision oncology for triple-negative breast cancer: Current advances and future directions

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Abstract

The aggressive and diverse subtype of breast cancer known as triple-negative breast cancer (TNBC) is devoid of HER2, progesterone, and oestrogen receptors. Due to the lack of actionable molecular targets, TNBC, which accounts for 15–20% of patients, is linked to a poor prognosis, early metastases, and few therapeutic choices. Although they are still the major therapeutic options, conventional treatments including radiation,chemotherapy, and surgery are limited by toxicity, drug resistance, and high recurrence rates.

The management of TNBC now has more options thanks to developments in artificial intelligence (AI) and precision medicine. Targeted treatments like PARP inhibitors and immune checkpoint inhibitors are supported by the discovery of actionable changes, such as BRCA1/2 mutations, made possible by genomic and proteomic analysis. By combining multi-omics, imaging, and clinical data, AI improves diagnosis, tumour subclassification, treatment response prediction, and medication repurposing. AI-driven precision medicine has great promise to enhance tailored treatment plans and clinical results in TNBC, despite obstacles pertaining to data privacy, equality, and legislation.

Keywords: Triple-Negative Breast Cancer, Precision Medicine, Artificial Intelligence, Targeted therapy, diagnosis of TNBC

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1. Introduction

Breast cancer (BC) is the second most prevalent cause of cancer-related death globally and the most often diagnosed malignancy in women. Hormone receptor (HR)–positive, HER2-positive, and triple-negative breast cancer (TNBC) are the three main subtypes of BC based on the expression of oestrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2). About 15–20% of instances of breast cancer are TNBC, which has a far worse prognosis than HR-positive tumours. Within three to five years of diagnosis, over half of patients experience a recurrence. The median overall survival for individuals with TNBC is still poor, at about 10.2 months, despite the availability of modern therapeutic options. TNBC is the only subtype of breast cancer for which there are no proven targeted treatments due to its distinctive lack of HER2 expression and low (<1%) ER and PR expression on immunohistochemistry. Biologically, TNBC is highly aggressive, often presenting as moderate- to high-grade tumors with high proliferative capacity. The combination of aggressive tumor biology and limited therapeutic options contributes to the unfavorable clinical outcomes observed in this subtype. While invasive ductal carcinoma is the most prevalent presentation of TNBC, there are a number of histological variations that may have unique biological traits and prognostic consequences.[1-3]

There are many intrinsic molecular subtypes of TNBC. Genes related to cell-cycle regulation and proliferation are expressed more often in basal-like subtypes (BL1 and BL2). Strong immune pathway activation and elevated tumor-infiltrating lymphocyte counts are characteristics of the immunomodulatory (IM) subtype. Transcriptional signalling mediated by androgen receptors drives the luminal androgen receptor (LAR) subtype. Angiogenesis, increased cell

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motility, and the epithelial–mesenchymal transition are associated with mesenchymal (M) and mesenchymal stem-like (MSL) subtypes. Additionally, some tumors remain unclassified due to the absence of distinct molecular features. RNA-based intrinsic subtyping is therapeutically useful in early-stage ER-positive breast cancer, but its applicability to TNBC is yet unknown. Immune-enriched basal-like tumours have greater pathological complete response rates in metastatic disease, although this does not always result in better event-free survival. Emerging proteomic and proteogenomic techniques are uncovering new, clinically significant vulnerabilities in TNBC beyond genomic and transcriptome characterisation, providing prospective paths for focused treatment development.[4-5]

TNBC emerged as a distinct breast cancer subtype nearly two decades ago following advances in gene expression profiling, which revealed that breast cancer comprises multiple molecularly diverse subtypes beyond those defined by ER and HER2 testing. Prognosis and, in certain situations, therapy response are strongly correlated with these inherent molecular classifications. It is anticipated that further molecular profiling will help clarify TNBC heterogeneity and facilitate the creation of more accurate treatment strategies. This section gives a general review of TNBC, describes the difficulties associated with its prognosis and therapy, and looks at precision medicine's role and the growing uses of artificial intelligence (AI) in oncology, with a focus on TNBC.[6]

2. Challenges in TNBC Treatment and Prognosis

Because of its unique molecular and clinical characteristics, TNBC presents significant prognostic problems. Its aggressive behaviour, early metastasis, and high recurrence rates—especially in the first three to five years following diagnosis—are caused by the absence of ER, PR, and HER2 expression, which restricts the adoption of targeted therapy. Consequently, compared to other subtypes of breast cancer, individuals with TNBC often have worse disease-free and overall survival.[7-9]

The molecular profile of TNBC is a key driver of prognosis and treatment selection, reflecting the disease's marked heterogeneity. Distinct molecular subtypes influence therapeutic response and survival outcomes, while specific biomarkers serve as important prognostic indicators. For example, PD-L1 expression is linked to better immunotherapy responses, while certain microRNAs, including miR-522, are linked to lower overall survival. Prognosis and treatment sensitivity are greatly impacted by genetic changes, especially BRCA1 and BRCA2 mutations; whereas BRCA-mutated tumours usually react favourably to platinum-based chemotherapy, resistance commonly develops. Targeted medicines, like as PARP inhibitors, which have demonstrated significant success in BRCA-mutated TNBC, have been made possible by the discovery of these genetic determinants. Using molecular biomarkers in clinical evaluation improves prognosis accuracy and facilitates the use of tailored treatment plans.[10,11]

Prognostic scoring methods that include clinical and molecular characteristics to better precisely predict outcomes have been developed to enhance patient care in TNBC. Conventional models stratify patients by risk based on variables such age, tumour size, histological grade, and lymph node status. Recent developments have greatly improved predicted accuracy by including transcriptomic and genomic data. By combining clinicopathological features with molecular insights, these models support refined risk stratification, personalized treatment planning, and informed decisions regarding neoadjuvant therapy and clinical trial enrollment. To improve survival rates in TNBC and advance precision oncology, these technologies must be continuously improved. One of the most aggressive kinds of breast cancer is TNBC, which has a dismal prognosis and few treatment choices. Since TNBC lacks clear molecular targets, it is more difficult to create effective targeted treatments than hormone receptor-positive or HER2-enriched breast tumours. As a result, chemotherapy continues to be the cornerstone of care, even though it is linked to serious toxicity, side effects, and inconsistent clinical outcomes. Furthermore, resistance mechanisms resulting from genetic changes, interactions with the tumour microenvironment, and cancer stem cell populations frequently impair treatment effectiveness, underscoring the critical need for innovative therapeutic approaches.[12,13]

Due to its high recurrence and metastatic potential even after first therapy, as well as its limited alternatives for advanced cancer, TNBC presents substantial problems. Because existing targeted medicines frequently fail to address all subtypes, its biological heterogeneity makes personalised therapy more difficult. Collaboration between academics, physicians, and industry is crucial as research focusses on new targets, subtype-specific medicines, and overcoming drug resistance. New approaches, such medicines based on nanotechnology, have the potential to increase effectiveness and lower treatment-related toxicity.[14]

Current therapy methods for TNBC have significant limitations, in addition to intrinsic treatment resistance and a dismal prognosis. Although surgery successfully eliminates primary tumours, it frequently results in local recurrence and cannot stop distant metastases. Although it raises the risk of harm to nearby healthy tissues, radiotherapy helps manage illness locally. Chemotherapy is still the mainstay of TNBC treatment, although significant side effects, including as haematological, gastrointestinal, and cardiac toxicities, as well as the development of multidrug resistance, often restrict its therapeutic efficacy. Although immunotherapy has improved outcomes in selected patients, its efficacy is restricted to specific subgroups and may cause immune-related adverse events. Although they provide potential

alternatives, targeted medicines like PARP and angiogenesis inhibitors are restricted by patient eligibility, toxicity, and acquired resistance. All of these issues highlight the critical need for novel, safer, and biologically based treatment approaches for TNBC.[15,16].

3. The Role of Precision Medicine in Oncology

Modern oncology has changed as a result of recent advances in cancer biology. Innovations like next-generation sequencing (NGS) and microarray technology, together with the Human Genome Project, have revolutionised cancer diagnosis, therapy, and classification. By customising treatments to each patient's unique genetic, environmental, and lifestyle characteristics, precision medicine has supplanted conventional uniform treatment methods, increasing therapeutic efficacy while lowering toxicity and medical expenses.[17]

Detailed characterisation of tumour biology and the discovery of driver mutations, copy number changes, and predictive biomarkers are made possible by comprehensive genomic profiling techniques, such as whole-exome sequencing, whole-genome sequencing, and gene expression analysis. Targeted treatments like trastuzumab for HER2-positive malignancies, cetuximab for KRAS wild-type colorectal cancer, and PARP inhibitors for BRCA-mutated tumours have been developed as a result of these advancements, and they frequently produce better results than traditional chemotherapy.[18]

There are still difficulties in spite of these achievements. Therapeutic resistance is often caused by tumour heterogeneity and clonal expansion, and widespread clinical use is hampered by infrastructure shortages, high prices, restricted access to genomic testing, and challenges in interpreting genetic variations. By combining genetic, clinical, and environmental data, large-scale projects like the NIH "All of Us" program seek to overcome these obstacles and advance precision oncology.[19]

The clinical significance of precision medicine is emphasised by TNBC. Conventional targeted treatments are limited by the lack of ER, PR, and HER2 expression, making chemotherapy the typical but less-than-ideal choice. Nevertheless, actionable subsets have been found by genomic profiling, such as PIK3CA-mutated malignancies that benefit with PI3K inhibitors and BRCA-mutated tumours that respond to PARP inhibitors. These biomarker-driven approaches highlight the potential of precision oncology in improving individualised treatment for TNBC by providing more potent and less harmful therapeutic options.[20]

4. Clinical Features and Diagnosis

ER, PR, and HER2 expression are absent in triple-negative breast cancer (TNBC), a unique and extremely aggressive form of the disease. Clinically, compared to other subtypes of breast cancer, it is linked to faster tumour development, a higher histological grade, and presentation at more advanced stages. Patients frequently exhibit skin alterations such dimpling, erythema, thickness, oedema, or a peau d'orange look in addition to a fast growing, hard, and uneven breast lump. There may also be anomalies of the nipples, such as discharge, scaling, or inversion. Axillary lymphadenopathy is often seen, indicating regional dissemination, even if breast discomfort is rare. Black or Hispanic people and those with BRCA1 mutations are more likely to develop TNBC, which disproportionately affects younger women under 40.[21]

Primary TNBC tumours are clinically obvious upon diagnosis because they are usually bigger, high-grade, and quickly multiplying. They are frequently found as interval cancers between normal mammography examinations. There is conflicting information on lymph node involvement at presentation; some studies report nodal metastasis often, even in tiny tumours, while others do not clearly link it to the basal-like subtype. When TNBC recurs, it is more likely to cause distant rather than local relapse, which mostly affects visceral organs such the brain, liver, and lungs rather than bone. Due to its aggressive biology, high risk of early recurrence, and tendency for distant metastasis, especially in the first three years following diagnosis, metastatic TNBC frequently manifests with multi-organ involvement. The poor clinical outcomes linked to TNBC are mostly caused by the more frequent involvement of the central nervous system[22,23] The diagnosis of TNBC follows a structured, stepwise approach beginning with clinical suspicion and radiological evaluation. Whereas ultrasonography usually shows a solid, hypoechoic lesion with irregular or angular boundaries, mammography frequently shows a dense mass with poorly defined or spiculated edges. Patients with multifocal illness or thick breast tissue benefit most from magnetic resonance imaging (MRI), which offers increased sensitivity for tumour identification.[24]

Core needle biopsy is used to provide a definitive diagnosis, enabling immunohistochemistry (IHC) investigation and histological assessment. TNBC is distinguished from subtypes that may be treated with hormonal or HER2-targeted therapy by the lack of ER, PR, and HER2 expression. In order to determine the extent of the illness and identify metastases, staging examinations are carried out utilising imaging modalities such CT, PET-CT, and bone scans. The AJCC TNM classification system, which takes into account tumour size, lymph node involvement, and the existence of distant metastases to inform prognosis and treatment planning, is used for disease staging.[25,26]

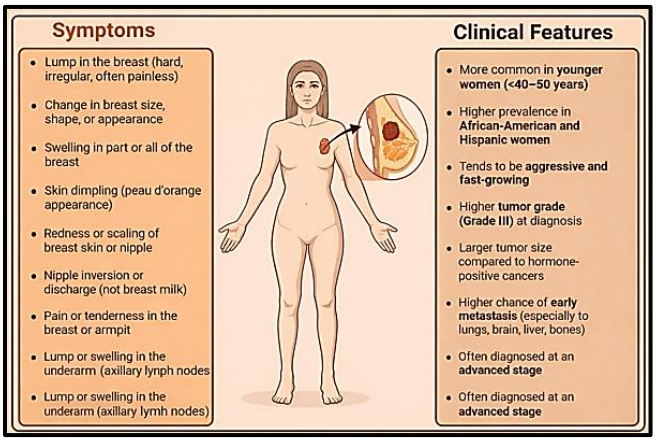

Figure 1: Clinical features and symptoms of triple-negative breast cancer[21,27]

5. Current Treatment Options and Limitations

Surgery, chemotherapy, radiation, immunotherapy, and new therapies such stem cell therapy, photodynamic therapy, and hyperthermia may all be administered to patients with TNBC. Chemotherapy is still the most often utilised strategy, but because TNBC is so heterogeneous, choosing a treatment needs carefully weighing its effectiveness, toxicity, and potential for overtreatment or undertreatment.[28]

Figure 2: Current treatment strategies for TNBC and its limitations

5.1. Role of surgery in TNBC

In order to prevent local recurrence, surgery—which can range from lumpectomy to mastectomy—is a crucial treatment for TNBC. It is frequently coupled with lymph node excision. Numerous studies show that radiation treatment after breast-conserving surgery yields survival results that are on par with mastectomy. Surgery may be performed as a palliative measure in metastatic illness to treat consequences such organ involvement, spinal cord compression, or fractures. However, oxidative stress can be brought on by surgical procedures, underscoring the potential advantages of postoperative antioxidant therapy.[29]

5.2. Radiation therapy

Compared to other subtypes of breast cancer, TNBC has a greater chance of both local and distant recurrence. Following surgery, radiotherapy is frequently used to destroy any remaining tumour cells in the breast and surrounding lymph nodes. However, resistance or recurrence may make radiation treatment inadequate on its own. Ongoing clinical trials, such as those assessing pembrolizumab with intraoperative irradiation, are examining this strategy in TNBC since it has been demonstrated that combining radiation with immunotherapy might improve anti-tumor immune responses.[30]

5.3. Chemotherapy approaches

Chemotherapy is still the cornerstone of treatment for TNBC; typical regimens include taxanes (such as paclitaxel and docetaxel) and anthracyclines (such as doxorubicin). The size and stage of the tumour determine whether to use adjuvant or neoadjuvant treatment. While chemotherapy offers limited benefit for very small tumors (<1 cm), larger tumors often respond well, with higher rates of pathological complete response (pCR)[31]

1. Anthracyclines: Through intercalation, these drugs prevent DNA replication, and by activating $CD8^+$ T cells, they stimulate the immune system. Despite their excellent response rates, cardiotoxicity and recurrence risk restrict their usage.[32]

2. Taxanes: Taxanes effectively kill tumour cells by interfering with microtubule dynamics and preventing angiogenesis. Widely used drugs include cabazitaxel, docetaxel, and paclitaxel; nab-paclitaxel was created to lessen toxicity. Particularly in metastatic TNBC, combination treatments include platinum and taxanes have demonstrated enhanced effectiveness.[33]

3. Platinum Agents: Medications that damage DNA, including carboplatin and cisplatin, work particularly well in tumours that have BRCA mutations or impaired DNA repair systems. Clinical research shows that platinum-based regimens, especially when paired with immunotherapy, boost pCR rates.[34]

6. Targeted Therapy in TNBC

1. PARP Inhibitors: Olaparib and talazoparib are examples of PARP inhibitors that have been approved by the FDA because to the high frequency of BRCA1/2 mutations in TNBC. These substances selectively target tumour cells with impaired DNA

repair pathways by acting through synthetic lethality. But their clinical use is mostly limited to patients with BRCA mutations, underscoring the need for strategies that expand their advantages to a larger TNBC group.[35]

2. EGFR Inhibitors: Overexpression of EGFR is common in several TNBC subtypes, making it a potential therapeutic target. Small-molecule inhibitors like gefitinib and erlotinib, as well as monoclonal antibodies like cetuximab, have been studied, frequently in conjunction with chemotherapy. New delivery methods based on nanotechnology seek to improve the effectiveness of EGFR-targeted siRNA or antibody treatments.[36]

3. VEGF Inhibitors: Vascular endothelial growth factor (VEGF) is critical for tumour angiogenesis and is associated with a poor prognosis in TNBC. Bevacizumab, an anti-VEGF monoclonal antibody, has increased pathological complete response rates when combined with neoadjuvant chemotherapy.[37]

4. Androgen Receptor (AR) Antagonists: Androgen receptor expression is seen in 12–36% of TNBC patients despite the absence of ER, PR, and HER2. In AR-positive TNBC, AR-targeted medications including enzalutamide and abiraterone acetate have shown clinical efficacy, providing a promising targeted therapeutic option.[38]

7. Immunotherapy in TNBC

When compared to other subtypes of breast cancer, triple-negative breast cancer (TNBC) is thought to be particularly immunogenic since it frequently shows greater levels of tumor-infiltrating lymphocytes and programmed death-ligand 1 (PD-L1) expression, which makes it a good candidate for immunotherapy. While CTLA-4 inhibitors like tremelimumab are being investigated to further boost immune activation, immune checkpoint inhibitors that target the PD-1/PD-L1 axis, such as pembrolizumab, nivolumab, and atezolizumab, restore T-cell-mediated antitumor responses and have received regulatory approval for PD-L1-positive TNBC. By combining strong cytotoxic drugs with monoclonal antibodies, antibody-drug conjugates (ADCs) have become a successful targeted approach. Sacituzumab govitecan, which targets Trop-2, has been licensed for metastatic TNBC and has shown notable survival advantages. Furthermore, by encouraging tumour growth, angiogenesis, and metabolic reprogramming, deregulation of the PI3K/AKT/mTOR signalling pathway is crucial to the development of TNBC. Despite this route's appeal as a therapeutic target, compensatory signalling and system complexity have hindered clinical translation. Although there are presently no PI3K/AKT/mTOR inhibitors that are particularly authorised for TNBC, a number of drugs are being investigated, and combination strategies—like combining immune checkpoint inhibitors with cytotoxic chemotherapy—show promise for improving therapeutic effectiveness.[39-43]

8. Limitations of Current Therapeutics

Although therapeutic advances have been made, TNBC management remains challenging. Unlike HER2-positive and hormone receptor-positive breast tumours, TNBC does not have well-defined molecular targets, which limits the application of targeted therapy. Consequently, despite its drawbacks, including toxicity, inconsistent effectiveness, treatment resistance, and poor results in advanced stages, chemotherapy remains the cornerstone of care. These challenges are intensified by the marked heterogeneity of TNBC, which includes multiple molecular subtypes without a universally effective therapeutic strategy, as well as a high propensity for recurrence and metastasis. Additional obstacles include resistance mechanisms driven by genetic alterations, cancer stem cells, and tumor–microenvironment interactions, along with significant adverse effects associated with surgery, radiotherapy, and systemic therapies. Overcoming these limitations will require biomarker-driven approaches, rational combination regimens, and innovative strategies such as antibody–drug conjugates, nanomedicine, and precision oncology.[9]

9. AI-Driven Approaches in TNBC

9.1. AI models for TNBC subtype classification and molecular profiling

With 98% cross-validation, 97% validation, and 91% external test accuracy, a multi-omics deep learning model that incorporates mRNA, miRNA, DNA methylation, mutation profiles, and MRI radiomics has outperformed single-omic techniques in the classification of TNBC molecular subtypes. Another method found two immune-related TNBC subtypes (S1 and S2) with an AUC of 0.76 using a Random Forest model based on 11 hub genes (such as LCK, STAT1, and IFNG) from TCGA-TNBC data; S1 was linked to improved treatment response and survival outcomes.[44,45]

10. Predictive Modelling for Treatment Response and Outcomes

AI-based histopathology models have a great deal of promise for forecasting TNBC patients' responses to neoadjuvant chemotherapy (NAC). NACNet achieved 90% accuracy, 96% sensitivity, 88% specificity, and an AUC of 0.82 by analysing whole-slide pictures to simulate spatial tumour microenvironment interactions using a graph convolution network and a histology-context aware transformer. Another method classified H&E biopsy tiles using a two-step machine learning procedure, using spatial graph characteristics to find unique TME-histological patterns indicative of NAC response. Furthermore, by evaluating tumour cellularity and volume, convolutional neural networks (CNNs) combined

with physiology-based modelling predicted each patient's response with good concordance.[46,47]

10.1. Integration of multi-omics data using AI

In order to enhance TNBC subtype categorisation and outcome prediction, AI is increasingly being utilised to combine imaging and multi-omics data (genomic, epigenomic, and transcriptomic). For instance, Bayesian optimisation is used in the multi-omics deep learning model presented in section 5.4.1 to improve network designs for more precise prognostic modelling. Other AI frameworks that use multi-omics inputs to prioritise candidates for epigenetic treatment include DeepDRK and gradient-boosted tree models like CHANCE. Notably, by combining mutation profiles, gene expression, and drug structural characteristics for targeted effectiveness in breast cancer subgroups, DeepDRK found possible drug-repositioning agents, such as the HDAC inhibitor vorinostat.[48]

10.2. AI in drug discovery and repurposing for TNBC

By discovering new treatment approaches and medication combinations, AI is transforming TNBC drug discovery. For instance, to predict synergistic medication pairings that cause pyroptosis, the BFReg-NN (biofactor-regulated neural network) was trained using omics and pharmacological data unique to TNBC. Mitoxantrone and gambogic acid were combined to create biomimetic nano-cocrystals (MG@PM), which demonstrated strong anti-tumor and immune-stimulating properties through pyroptosis activation. Beyond TNBC, medication repurposing is further supported by multi-omics AI frameworks like DeepDRK and CHANCE. While CHANCE uses gradient-boosted trees and interaction networks to find anticancer potential in non-oncological medications, DeepDRK predicts drug sensitivity by combining intricate biological and chemical factors.[49]

11. Case Studies and Current Research

Recent advancements in the area have illuminated new therapy choices, biomarkers, and diagnostic methods since TNBC is an aggressive malignancy. This article examines important case reports and ongoing research projects that are changing the landscape of TNBC therapy.

11.1. TILs as predictive and prognostic indicators in TNBC

High numbers of tumor-infiltrating lymphocytes (TILs) were strongly linked to improved outcomes, with 95% of stage I patients with high TILs surviving five years compared to 82% with low TILs, according to a multicenter analysis of 1,966 early-stage TNBC patients. These results imply that TILs may be an affordable biomarker for identifying low-risk individuals who might not need chemotherapy. TILs are now being validated in a variety of groups, including African American women, who are more likely to develop TNBC.[49,50]

11.2. Targeted therapy with antibody–drug conjugates in metastatic TNBC

Sacituzumab govitecan (Trodelvy®), an antibody–drug conjugate (ADC) that targets Trop-2, which is overexpressed in almost 80% of TNBC patients, and delivers the cytotoxic chemical SN-38 directly to cancer cells, was approved in 2020, marking a significant advancement in metastatic TNBC. With a median overall survival of 12.1 months against 6.7 months and a median progression-free survival of 5.6 months versus 1.7 months when compared to conventional chemotherapy, the phase III ASCENT study showed that sacituzumab govitecan considerably improved results. These findings demonstrate how ADCs can improve effectiveness while lowering systemic toxicity, advancing precision oncology in TNBC.[51]

11.3. Checkpoint inhibition in TNBC: Pembrolizumab

The PD-1 inhibitor pembrolizumab (Keytruda®) has revolutionised the treatment of PD-L1-positive TNBC. Pathological complete response (pCR) rates in high-risk early-stage TNBC were considerably higher in the KEYNOTE-522 study when pembrolizumab was added to neoadjuvant chemotherapy (64.8% versus 51.2% with chemotherapy alone). After the KEYNOTE-355 research shown improvements in progression-free and overall survival when paired with chemotherapy, pembrolizumab was eventually designated as the standard of treatment for PD-L1-positive metastatic TNBC. Ongoing studies like Saci-IO are investigating pembrolizumab and sacituzumab govitecan combos for PD-L1-negative patients in order to overcome immunotherapy resistance. TNBC patients with BRCA1/2 mutations benefit from PARP inhibitors, such as talazoparib and olaparib; the OlympiAD research found that olaparib had a median progression-free survival of 7.0 months compared to 4.2 months with conventional chemotherapy. However, their wider relevance is limited since only 15–20% of TNBC patients have BRCA mutations. To increase their therapeutic potential, current research is investigating synthetic lethality techniques, such as combining PARP inhibitors with PI3K or AKT inhibitors.[52-54]

11.4. Real-world data and retrospective analyses in TNBC

The median overall survival increased from 10.9 to 11.9 months in a retrospective analysis of 2,534 metastatic TNBC patients (2011–2022), despite the introduction of PARP inhibitors, ADCs, and immune checkpoint inhibitors. This emphasises the ongoing problem of medication resistance and the pressing need for new potent first-line treatments. Data from the real world also show differences in access to new therapies, especially in low-resource environments where sophisticated diagnostics like next-generation sequencing for BRCA testing are frequently not available.[55]

12. Novel Therapeutic Approaches and Combinations

Novel combination therapy are being investigated in current clinical trials to address the genomic heterogeneity of TNBC. Early findings from the phase II Dato-DXd study, which assesses durvalumab (a PD-L1 inhibitor) in combination with datopotamab deruxtecan (a TROP2-targeted ADC) in severely pretreated metastatic TNBC, are encouraging. Furthermore, in order to overcome resistance to single-agent therapy, mTOR inhibitors for mesenchymal subtypes and receptor tyrosine kinase (RTK) inhibitors for basal-like TNBC target certain signalling pathways. Additionally, early-phase trials are evaluating the possibility of bispecific antibodies and chimeric antigen receptor (CAR) T-cell treatments as novel immunotherapeutic strategies for TNBC.[56,57]

13. Conclusion

Through integrating multi-omics data and sophisticated prediction models to enhance diagnosis, tailor treatment, and speed up drug development, artificial intelligence has the potential to revolutionise TNBC management. The aggressive and diverse character of TNBC may be addressed by these developments, perhaps leading to better patient outcomes. Informed consent, data bias, accountability, data privacy, and regulatory compliance are just a few of the ethical, legal, and sociological issues that must be carefully considered for their successful implementation. It is crucial to encourage patient involvement, fair access, and trust, especially for marginalised groups. To guarantee the responsible and efficient use of AI in TNBC care, ethical-by-design frameworks, multistakeholder cooperation, different datasets, inclusive development, and harmonised legislation will be essential.

14. Source of Funding

None.

15. Conflict of Interest

None.

References

1. De Laurentiis M, Cianniello D, Caputo R, Stanzione B, Arpino G, Cinieri S, et al. Treatment of triple negative breast cancer (TNBC): Current options and future perspectives. *Cancer Treat Rev*. 2010;36(3):80-6. https://doi:10.1016/S0305-7372(10)70025-6
2. Thanopoulou E, Khader L, Caira M, Wardley A, Ettl J, Miglietta F, et al. Therapeutic strategies for the management of hormone receptor-positive, human epidermal growth factor receptor 2-positive (HR+/HER2+) breast cancer: A review of the current literature. *Cancers (Basel)*. 2020;12(11):1–29. https://doi:10.3390/cancers12113317
3. Cserni G, Quinn CM, Foschini MP, Bianchi S, Callagy G, Chmielik E, et al. Triple-negative breast cancer histological subtypes with a favourable prognosis. *Cancers (Basel)*. 2021;13(22):56-97. https://doi:10.3390/cancers13225694
4. Lehmann BD, Colaprico A, Silva TC, Chen J, An H, Ban Y, et al. Multi-omics analysis identifies therapeutic vulnerabilities in triple-negative breast cancer subtypes. Nat Commun. 2021 Nov 1;12(1):6276.
5. Lehmann BD, Colaprico A, Silva TC, Chen J, An H, Ban Y, et al. Multi-omics analysis identifies therapeutic vulnerabilities in triple-negative breast cancer subtypes. *Nat Commun*. 2021;12(1):
6. Asleh K, Riaz N, Nielsen TO. Heterogeneity of triple negative breast cancer: Current advances in subtyping and treatment implications. *J Exp Clin Cancer Res*. 2022;41(1):265. https://doi:10.1186/s13046-022-02476-1
7. Collignon J, Lousberg L, Schroeder H, Jerusalem G. Triple-negative breast cancer: Treatment challenges and solutions. *Breast Cancer Targets Ther*. 2016;8:93–107. https://doi:10.2147/BCTT.S69488
8. Xiong N, Wu H, Yu Z. Advancements and challenges in triple-negative breast cancer: a comprehensive review of therapeutic and diagnostic strategies. *Front Oncol*. 2024;14: https://doi:10.3389/fonc.2024.1405491
9. Obidiro O, Battogtokh G, Akala EO. Triple Negative Breast Cancer Treatment Options and Limitations: Future Outlook. Pharmaceutics. 2023;15(7):1796. https://doi:10.3390/pharmaceutics15071796
10. Mylavarapu S, Das A, Roy M. Role of BRCA mutations in the modulation of response to platinum therapy. *Front Oncol*. 2018;8:16. https://doi:10.3389/fonc.2018.00016
11. De Luca P, De Siervi A. Critical role for BRCA1 expression as a marker of chemosensitivity response and prognosis. *Front Biosci Elit*. 2016;8(1):72–83. https;//doi:10.2741/E752
12. Sukumar J, Gast K, Quiroga D, Lustberg M, Williams N. Triple-negative breast cancer: promising prognostic biomarkers currently in development. *Expert Rev Anticancer Ther*. 2021;21(2):135–48. https://doi:10.1080/14737140.2021.1840984
13. Toss A, Cristofanilli M. Molecular characterization and targeted therapeutic approaches in breast cancer. *Breast Cancer Res*. 2015;17(1): https;//doi:10.1186/s13058-015-0560-9
14. De Francesco EM, Cirillo F, Vella V, Belfiore A, Maggiolini M, Lappano R. Triple-negative breast cancer drug resistance, durable efficacy, and cure: how advanced biological insights and emerging drug modalities could transform progress. *Expert Opin Ther Targets*. 2022;26(6):513–35. https;//doi:10.1080/ 14728222.2022.2094762
15. Dias MP, Moser SC, Ganesan S, Jonkers J. Understanding and overcoming resistance to PARP inhibitors in cancer therapy. *Nat Rev Clin Oncol*. 2021;18(12):773–91. https://doi:10. 1038/s41571-021-00532-x
16. Liu Y, Hu Y, Xue J, Li J, Yi J, Bu J, et al. Advances in immunotherapy for triple-negative breast cancer. *Mol Cancer*. 2023;22(1): https://doi:10.1186/s12943-023-01850-7
17. Wang Y, Zheng D. The importance of precision medicine in modern molecular oncology. *Clin Genet*. 2021;100(3):248–57. https://doi:10.1111/cge.13998
18. Jiang M, Yang J, Li K, Liu J, Jing X, Tang M. Insights into the theranostic value of precision medicine on advanced radiotherapy to breast cancer. *Int J Med Sci*. 2021;18(3):626–38. https;//doi:10.7150/ijms.49544
19. Rizvi N, Lyu H, Vaidya L, Wu XC, Miele L, Yu Q. Genomic and Socioeconomic Determinants of Racial Disparities in Breast Cancer Survival: Insights from the All of Us Program. *Cancers (Basel)*. 2024;16(19):3294. https://doi:10.3390/cancers 16193294
20. Principe DR. Precision Medicine for BRCA/PALB2-Mutated Pancreatic Cancer and Emerging Strategies to Improve Therapeutic Responses to PARP Inhibition. Cancers (Basel). 2022;14(4):897. https://doi:10.3390/cancers14040897
21. Tan T, Dent R. Triple-Negative Breast Cancer: Clinical Features. Triple-Negative Breast Cancer A Clin Guid. 2018;23–32. https;//doi:10.1158/1078-0432.CCR-06-3045
22. Weledji EP, Tambe J. Breast Cancer Detection and Screening. *Med Clin Rev*. 2018;04(02): https://doi:10.217 67/2471299X.1000071
23. Sjödahl G, Eriksson P, Lövgren K, Marzouka NAD, Bernardo C, Nordentoft I, et al. Discordant molecular subtype classification in

the basal-squamous subtype of bladder tumors and matched lymph-node metastases. *Mod Pathol*. 2018;31(12):1869–81. https;//doi:10.1038/s41379-018-0096-5

24. Sha YS, Chen JF. MRI-based radiomics for the diagnosis of triple-negative breast cancer: a meta-analysis. *Clin Radiol*. 2022;77(9):655–63. https;//doi:10.1016/j.crad.2022.04.015
25. Schneeweiss A, Denkert C, Fasching PA, Fremd C, Gluz O, Kolberg-Liedtke C, et al. Diagnosis and Therapy of Triple-Negative Breast Cancer (TNBC) - Recommendations for Daily Routine Practice. *Geburtshilfe Frauenheilkd*. 2019;79(6):605–17. https://doi:10.1055/a-0887-0285
26. Groheux D, Hindie E. Breast cancer: initial workup and staging with FDG PET/CT. *Clin Transl Imag*. 2021;9(3):221–31. https;//doi:10.1007/s40336-021-00426-z
27. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: Clinical features and patterns of recurrence. *Clin Cancer Res*. 2007;13(15):4429–34. https://doi:10.1158/1078-0432.CCR-06-3045
28. Vinchurkar K, Doke R, Joshi S, Muleva G, Singh S, Singh S. Artificial intelligence-driven precision medicine for triple negative breast cancer. In: Artificial Intelligence-Driven Precision Medicine for Triple Negative Breast Cancer. Elsevier; 2026:113–32.
29. Fancellu A, Houssami N, Sanna V, Porcu A, Ninniri C, Marinovich ML. Outcomes after breast-conserving surgery or mastectomy in patients with triple-negative breast cancer: meta-analysis. *Br J Surg*. 2021;108(7):760–8. https://doi:10.1093/bjs/znab145
30. Moran MS. Radiation therapy in the locoregional treatment of triple-negative breast cancer. *Lancet Oncol*. 2015;16(3):e113–22. https://doi:10.1016/S1470-2045(14)71104-0
31. Marra A, Curigliano G. Adjuvant and Neoadjuvant Treatment of Triple-Negative Breast Cancer with Chemotherapy. Cancer J (United States). 2021;27(1):41–9. https;//doi:10.1097/PPO.0000000000000498
32. Das C, Adhikari S, Bhattacharya A, Chakraborty S, Mondal P, Yadav SS, et al. Epigenetic-Metabolic Interplay in the DNA Damage Response and Therapeutic Resistance of Breast Cancer. *Cancer Res*. 2023;83(5):657–66. https://doi:10.1158/0008-5472.CAN-22-3015
33. Sharifi-Rad J, Quispe C, Patra JK, Singh YD, Panda MK, Das G, et al. Paclitaxel: Application in Modern Oncology and Nanomedicine-Based Cancer Therapy. *Oxid Med Cell Longev*. 2021;2021.
34. Basourakos SP, Li L, Aparicio AM, Corn PG, Kim J, Thompson TC. Combination Platinum-based and DNA Damage Response-targeting Cancer Therapy: Evolution and Future Directions. Curr Med Chem. 2016;24(15): https://doi:10.2174/0929867323666161214114948
35. Beniey M, Haque T, Hassan S. Translating the role of PARP inhibitors in triple-negative breast cancer. Oncoscience. 2019;6(1–2):287–8. https://doi:10.18632/oncoscience.474
36. Lev S. Targeted therapy and drug resistance in triple-negative breast cancer: The EGFR axis. Biochem Soc Trans. 2020;48(2):657–65. https://doi:10.1042/BST20191055
37. Xie W, Zhang Y, Zhang S, Wang F, Zhang K, Huang Y, et al. Oxymatrine enhanced anti-tumor effects of Bevacizumab against triple-negative breast cancer via abating Wnt/β-Catenin signaling pathway. Am J Cancer Re. 2019;9(8):1796–814. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31497360%0A http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC6726698
38. Miller K, Yardley DA, Eakle J, Schwartzberg LS, O'Shaughnessy J, Gradishar W., et al. Enzalutamide for the treatment of androgen receptor-expressing triple-negative breast cancer. J Clin Oncol. 2018;36(9):884–90. Available from: http://ascopubs.org/doi/pdf/10.1200/JCO.2016.71.3495
39. Thomas R, Al-Khadairi G, Decock J. Immune Checkpoint Inhibitors in Triple Negative Breast Cancer Treatment: Promising Future Prospects. Front Oncol. 2021;10.
40. Zhang M, Song J, Yang H, Jin F, Zheng A. Efficacy and safety of PD-1/PD-L1 inhibitors in triple-negative breast cancer: a systematic review and meta-analysis. *Acta Oncol (Madr)*. 2022;61(9):1105–15. https://doi:10.1080/0284186X.2022.2106795
41. Page DB, Beal K, Linch SN, Spinelli KJ, Rodine M, Halpenny D, et al. Brain radiotherapy, tremelimumab-mediated CTLA-4-directed blockade +/− trastuzumab in patients with breast cancer brain metastases. NPJ Breast Cancer. 2022;8(1):50. https://doi:10.1038/s41523-022-00404-2
42. Sakach E, Sacks R, Kalinsky K. Trop-2 as a Therapeutic Target in Breast Cancer. *Cancers (Basel)*. 2022;14(23): https://doi:10.3390/cancers14235936.
43. Khan MA, Jain VK, Rizwanullah M, Ahmad J, Jain K. PI3K/AKT/mTOR pathway inhibitors in triple-negative breast cancer: a review on drug discovery and future challenges. *Drug Discov Today*. 2019;24(11):2181–91. https://doi:10.1016/j.drudis.2019.09.001
44. Yang S, Wang Z, Wang C, Li C, Wang B. Comparative Evaluation of Machine Learning Models for Subtyping Triple-Negative Breast Cancer: A Deep Learning-Based Multi-Omics Data Integration Approach. *J Cancer*. 2024;15(12):3943–57.
45. Chen Z, Wang M, De Wilde RL, Feng R, Su M, Torres-de la Roche LA, et al. A Machine Learning Model to Predict the Triple Negative Breast Cancer Immune Subtype. *Front Immunol*. 2021;12:
46. Li Q, Teodoro G, Jiang Y, Kong J. NACNet: A histology context-aware transformer graph convolution network for predicting treatment response to neoadjuvant chemotherapy in Triple Negative Breast Cancer. Comput Med Imag Graph. 2024;118. https://doi:10.1016/j.compmedimag.2024.102467
47. Fisher TB, Saini G, Rekha TS, Krishnamurthy J, Bhattarai S, Callagy G, et al. Digital image analysis and machine learning-assisted prediction of neoadjuvant chemotherapy response in triple-negative breast cancer. *Breast Cancer Res*. 2024;26(1): https://doi:10.1186/s13058-023-01752-y
48. Salvati A, Melone V, Giordano A, Lamberti J, Palumbo D, Palo L, et al. Multi-omics based and AI-driven drug repositioning for epigenetic therapy in female malignancies. J Transl Med. 2025;23(1):837.
49. Stovgaard ES, Nielsen D, Hogdall E, Balslev E. Triple negative breast cancer–prognostic role of immune-related factors: a systematic review. Acta Oncol (Madr). 2018;57(1):74–82. Available from: https://cancerblog.mayoclinic.org/2024/04/25/ new-study-finds-triple-negative-breast-cancer-tumors-with-an-increase-in-immune-cells-have-lower-risk-of-recurrence-after-surgery/
50. Leon-Ferre RA, Jonas SF, Salgado R, Loi S, De Jong V, Carter JM, et al. Tumor-Infiltrating Lymphocytes in Triple-Negative Breast Cancer. Jama. 2024;331(13):1135–44. https://doi:10.1001/jama.2024.3056
51. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. *N Engl J Med*. 2021;384(16):1529–41. https://doi:10.1056/NEJMoa2028485
52. Schmid P, JCortes J, Pusztai L, McArthur H, Kümmel S, Bergh J, Carsten Denkert M. Pembrolizumab for Early Triple-Negative Breast Cancer. *N Engl J Med*. 2020;382(26): Available from: http://www.nejm.org/doi/10.1056/NEJMc2006684
53. Mark Robson, M.D., Seock-Ah Im, M.D., Ph.D., Elżbieta Senkus, M.D., Ph.D., Binghe Xu, M.D., Ph.D., Susan M. Domchek, M.D., Norikazu Masuda, M.D., Ph.D., Suzette Delaloge MD. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. N Engl J Med. 2017;377(17):1700–700. Available from: http://www.nejm. org/doi/10.1056/NEJMx170012
54. Emara HM, Allam NK, Youness RA. A comprehensive review on targeted therapies for triple negative breast cancer: an evidence-based treatment guideline. *Discov Oncol*. 2025;16(1):547. https://doi:10.1007/s12672-025-02227-6
55. Punie K, Kurian AW, Ntalla I, Sjekloca N, Estrin A, Dabrowski EC, et al. Unmet need for previously untreated metastatic triple-negative

breast cancer: a real-world study of patients diagnosed from 2011 to 2022 in the United States. Oncologist. 2025;30(3):1-12. https://doi.org/10.1093/oncolo/oyaf034

56. Abuhadra N, Sun R, Bassett RL, Huo L, Chang JT, Teshome M, et al. Targeting chemotherapy resistance in mesenchymal triple-negative breast cancer: a phase II trial of neoadjuvant angiogenic and mTOR inhibition with chemotherapy. *Invest New Drugs*. 2023;41(3):391–401. https://doi:10.1007/s10637-023-01357-4
57. Zhang HP, Jiang RY, Zhu JY, Sun KN, Huang Y, Zhou HH, et al. PI3K/AKT/mTOR signaling pathway: an important driver and therapeutic target in triple-negative breast cancer. *Breast Cancer*. 2024;31(4):539–51. https://doi:10.1007/s12282-024-01567-5

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