Tailoring Treatment: Chemotherapy and Targeted Therapies in Breast Cancer Subtypes

Abstract: The profound heterogeneity of breast cancer fundamentally drives the differences in disease progression and treatment response, promoting molecular subtype-oriented treatment to become a new clinical paradigm. This article systematically analyzes the differences in chemotherapy and targeted therapy classification among the three major subtypes of HR+, HER2+, and TNBC, emphasizing the turning point value of molecular typing based on ER/PR/HER2 status for individualized decision-making. Heterogeneous management requires precise anchoring of subtype characteristics to balance efficacy and toxicity. Breakthroughs in genomic technology are accelerating the progress of targeted therapy: The Luminal subtype requires the optimization of the CDK4/6 inhibitor synergy strategy; The resolution of HER2+ group drug resistance depends on stratified treatment. Immune and PARP inhibitors in the TNBC field reshape the therapeutic landscape. The current bottlenecks are mainly focused on the differences in biomarker accessibility, the lack of analysis of drug resistance mechanisms, and the dynamic interference of heterogeneity. This review provides an evidence-based framework for individualized treatment and concretizes the future breakthrough path - achieving a strategic leap from passive management to precise regulation through intelligent dynamic monitoring to optimize survival outcomes.

Keywords: Breast Cancer, Chemotherapy, Targeted Therapies, Molecular Profiling, Personalized Medicine.

1. Introduction

Breast cancer is essentially a disease driven by extensive and profound molecular and phenotypic heterogeneity. This inherent diversity dominates the clinical course, profoundly influencing the treatment response and determining the long-term prognosis. This biological complexity necessitates subdivision into molecularly distinct subtypes with distinct molecular characteristics. The core classification framework currently relied upon for clinical decision-making is based on hormone receptors (estrogen receptor ER; The expression status of progesterone receptor PR and human epidermal growth factor receptor 2 (HER2) defines breast cancer as Luminal A, Luminal B, HER2-enriched and triple-negative breast cancer (TNBC), etc. [1, 2]. The significance of deeply grasping these subtype-specific differences far exceeds the theoretical cognitive scope. It directly determines the choice of clinical treatment pathways and is inseparable from the core logic of rationally designing targeted therapies - these therapies aim to precisely intervene in the unique dysregulated molecular pathways in different subtypes.

It is precisely driven by such insights that the treatment concept of breast cancer has undergone a profound paradigm shift, with its core shifting towards precision medicine. This framework is dedicated to transcending the traditional "one-size-fits-

all" model and strategically formulating treatment decisions based on integrated individualized patient data (including genomic maps, mature biomarkers, and phenotypic characteristics) [3, 4]. The practical transformation of precision medicine in the field of breast cancer has achieved a revolutionary breakthrough. The most representative milestone is the advent of anti-HER2 drugs such as trastuzumab - this breakthrough has completely rewritten the once severe survival expectations of HER2-positive patients and significantly increased their chances of survival [5]. Meanwhile, continuous and in-depth research has been constantly expanding the therapeutic Arsenal, providing innovative drugs and complex combination regimens, offering key means to combat certain highly invasive and difficult-to-treat subtypes (such as TNBC) [6].

However, despite these commendable and considerable advancements, severe challenges still exist. The deep heterogeneity of breast cancer continuously weakens the efficacy of existing therapies for a considerable number of patients. The inherent or acquired drug resistance mechanisms have not been fully elucidated to date, making effective responses extremely difficult [7, 8]. To make matters worse, the crucial yet often underestimated complex association between internal tumor heterogeneity (the diversity of clonal populations within a single individual) and therapeutic effects urgently requires systematic research. Clarifying the core molecular mechanisms behind different therapeutic response spectra has become an unavoidable key frontier exploration direction [9]. Given these outstanding complexities and their profound impact on patient outcomes, this review aims to launch a critical integration - focusing on the current understanding of the heterogeneity of breast cancer. We will particularly analyze its key implications to optimize the clinical application of traditional chemotherapy and molecular targeted drugs. By delving deeply into the strategic complexity of precision medicine in the field of breast cancer, we hope that this analysis is not merely a summary but also aims to serve as a catalyst for optimizing future research directions and guiding the evolution of evidence-based and adaptive clinical paradigms.

2.Body

2.1. Chemotherapy Regimens by Breast Cancer Subtype

Breast cancer shows significant molecular heterogeneity, and individualized treatment plans must be formulated based on specific molecular subtypes. The main subtypes include Luminal A type, Luminal B type, HER2-enriched type and triple-negative breast cancer (TNBC). Luminal A tumors are characterized by high estrogen receptor (ER) expression and low proliferative activity, and respond well to endocrine therapy (such as tamoxifen or aromatase inhibitors) [10]. In contrast, Luminal B type has both high proliferative activity and common HER2 co-expression, and often requires chemotherapy combined with targeted treatments such as trastuzumab [11].

Her2-enriched breast cancer is highly invasive. Its treatment requires the integration of anti-HER2-targeted biological agents on the basis of chemotherapy, which significantly improves the overall survival rate [12]. TNBC has become a clinical challenge due to the absence of hormone receptors and HER2 expression, and there is an urgent need for strong chemotherapy regimens (such as taxanes combined with anthracyclines) [11][13]. This subtype has a particularly high recurrence risk and is particularly worthy of vigilance. It is promoting breakthrough explorations in immunotherapy and new molecular targeted drugs [14]. With the continuous deepening of research on the molecular mechanisms of breast cancer, chemotherapy strategies are accelerating towards a biomarker-driven individualized paradigm - this dynamic evolution requires that treatment pathways always be anchored to the biological essence of tumors [15].

2.1.1. Triple-Negative Breast Cancer (TNBC)

Overview of chemotherapy options: Anthracyclines, taxanes, and platinum agents.

Triple-negative breast cancer (TNBC) is characterized by the deletion of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), accounting for approximately 10-20% of all breast cancer cases [16][17]. The treatment system for this subtype is based on systemic chemotherapy, among which anthracyclines, taxanes and platinum-based drugs constitute the core therapeutic pillars [18].

Anthracycline drugs (such as doxorubicin and epirubicin) efficiently induce tumor cell apoptosis through DNA intercalation and topoisomerase II inhibition [19], but their dose-cumulative cardiotoxicity significantly limits clinical application, and strict cardiac function monitoring and lifelong dose upper limit setting are required [20]. Taxanes (paclitaxel, docetaxel) block the mitosis process through microtubule stabilization mechanisms [21], but toxicity such as dose-dependent peripheral neuropathy and neutrophilia often forces adjustments to treatment regimens [22].

Platinum-based preparations (cisplatin, carboplatin) have shown special value in the treatment of homologous recombination repair of defective TNBC due to their ability to induce DNA cross-linking damage [23][24], but their wide application is limited by nephrotoxicity, bone marrow suppression and acquired drug resistance mechanisms [18]. This current situation requires the establishment of a dynamic decision-making model: integrating the molecular characteristics of patients (such as BRCA mutation status), real-time treatment response and cumulative toxicity spectrum, and ultimately achieving the optimization of risk and benefit [17][20].

2.1.2. HER2-Positive Breast Cancer

The combination of taxanes and carboplatin for HER2-targeted therapy has become a key strategy for HER2-positive breast cancer. Paclitaxel derivatives (such as paclitaxel/docetaxel) block the cell cycle process by interfering with microtubule dynamics and induce tumor cell apoptosis [21]. When combined with the platinum-based drug carboplatin, its synergistic effect significantly enhances the anti-tumor effect, especially having special value for patients with aggressive subgroups [25].

The latest research has confirmed that adding carboplatin to tax-based regimens can improve the survival outcomes of patients with residual lesions after neoadjuvant therapy [26]. Typical clinical evidence shows that the trastuzumab combined with taxanes/carboplatin regimen significantly improves the pathological complete response rate (pCR) compared with taxanes monotherapy [27]. Further research confirmed that this combination therapy can significantly prolong the overall survival period of patients [28].

It is worth noting that the triple regimen may lead to a significant aggravation of hematological toxicity (especially myelosuppression-related neutropenia) [22]. This has prompted current research to focus on the optimization of dose-intensive regimens and the design of sequential treatment, aiming to preserve therapeutic efficacy while controlling the risk of adverse reactions [29]. This multi-modal collaborative strategy that integrates chemotherapy and targeted therapy is creating a new pattern for intensive treatment of HER2-positive breast cancer.

2.1.3. Hormone Receptor-Positive Breast Cancer (HR+)

Insights on chemotherapy use limited to high-risk cases.

Hormone receptor-positive (HR+) breast cancer is characterized by the expression of estrogen receptor (ER) and/or progesterone receptor (PR), accounting for approximately 70% of all breast cancer cases. The management of this type of tumor is based on an endocrine therapy system. Selective estrogen receptor modulators (SERMs) and aromatase inhibitors and other drugs significantly improve patient survival [30][31]. Chemotherapy is mainly applied to high-risk patient groups, especially when there are invasive biological characteristics (such as high proliferative activity, vascular invasion) or high recurrence risk predictive factors (such as high scores in 21-gene testing) [32][33].

Clinical decision-making requires the integration of multi-dimensional parameters: primary tumor burden (≥5cm), histological grade (grade III), lymph node metastasis range (≥4 positive), and the patient's tolerance basis jointly constitute key considerations [34]. For instance, for patients with the above-mentioned high-risk factors, adjuvant chemotherapy can significantly reduce the risk of long-term recurrence [35]. The latest Phase III clinical trial has confirmed that in specific HR+ high-risk subgroups - especially those with a tendency to resistance to primary endocrine therapy - chemotherapy combined with endocrine regimens can

significantly improve disease-free survival [36][37]. Therefore, although endocrine therapy continues to dominate the treatment landscape of HR+ breast cancer, chemotherapy still becomes a core strategy for avoiding recurrence risk in precisely screened high-risk patients through rigorous benefit-risk assessment [35].

2.2. Targeted Therapy Drugs Based on Molecular Targets

Targeted therapy has become a strategic pillar of modern oncology, driving the treatment paradigm to shift from traditional chemotherapy to precise strategies focusing on tumor-specific molecular aberrations. This strategy significantly improves the clinical outcomes of various cancers by developing specific drugs that selectively block key pathways for cancer cell survival and proliferation, such as small molecule inhibitors and monoclonal antibodies [3][38]. Based on genomic mapping to identify clinically intervenable targets, it helps to precisely match the optimal treatment plan, improving therapeutic effects while reducing the risks of traditional treatments [39][40].

However, the evolution of drug resistance mechanisms poses significant clinical challenges: processes such as secondary target mutations, activation of bypass signaling pathways, and reprogramming of the tumor microenvironment can weaken the initial treatment response [41]. To break through this bottleneck, the research frontier is exploring combined strategies of multi-pathway coordinated blocking (such as dual inhibition of EGFR/MEK) to reverse drug resistance by overcoming compensatory signal transduction [42]. It is worth noting that biomarker-driven clinical research design is becoming the key to optimizing decision-making - by enriching sensitive populations and dynamically monitoring the evolution of drug-resistant clones to ensure the maximization of therapeutic benefits [43][44]. With the deepening of understanding of tumor heterogeneity, the development of allosteric inhibitors and the iteration of real-time adaptive treatment regimens will continue to drive the expansion of the territory of precision cancer treatment.

2.2.1. HER2-Positive Breast Cancer

Efficacy of trastuzumab and pertuzumab

Trastuzumab (Herceptin®) and Pertuzumab (Perjeta®) jointly lay the foundation for targeted therapy of HER2-positive breast cancer and profoundly reshape patients' survival expectations. Trastuzumab, as a humanized monoclonal antibody targeting the extracellular domain IV domain of the HER2 receptor, mediates tumor clearance by blocking pro-survival signaling pathways such as PI3K-AKT/mTOR and activating antibody-dependent cytotoxicity (ADCC) [45]. Key clinical studies have confirmed that the combination of this drug and chemotherapy significantly prolongs the median overall survival (by 37%) and disease-free survival (with an improvement rate of ≥40%) in patients with metastatic and early-stage diseases [46][47].

Pertuzumab inhibits the formation of HER2-HER3 heterodimers by specifically binding to the HER2 receptor II domain, and constructs a spatially complementary dual blocking mechanism with trastuzumab [48]. This synergistic effect has led to a breakthrough in the pathological complete response rate (pCR) in neoadjuvant therapy - 39-60% for dual-target regimens, significantly higher than the benchmark of 21-22% for single-target therapy [49]. Real-world evidence-based further verified its clinical tolerability and benefit balance, which was manifested as an extended median progression-free survival of 5.8 months (hazard ratio HR=0.62), and the incidence of grade ≥3 treatment-related adverse events was controlled within the 10% threshold [50].

The evolution of drug resistance remains a core challenge at present, mainly involving three interrelated aspects: acquired mutations in the HER2 kinase domain (such as L755S/T798I), persistent activation of the PI3K pathway induced by PTEN deletion, and compensatory upregulation of the IGF-1R signaling axis [51][52]. The research frontier is focusing on the precise clearance ability of the new generation of antibody-drug conjugates (such as T-DXd) against drug-resistant clones, exploring the sequential combination strategy of PI3K/mTOR inhibitors and dual-target therapy, and developing adaptive treatment regimens based on dynamic monitoring of circulating tumor DNA (ctDNA) to break through the current treatment bottleneck.

2.2.2. BRCA-Mutated Breast Cancer

Role of PARP inhibitors in treatment.

Breast cancer carrying BRCA1/2 gene mutations has defects in homologous recombination repair (HRR), which leads to high sensitivity of tumor cells to DNA damage agents. Polyadenosine diphosphate ribose polymerase (PARP) inhibitors precisely target this weakness by synthesizing lethal effects - drugs binding to PARP to form toxic complexes (PARP trapping), blocking DNA single-strand break repair and triggering replication fork collapse, ultimately promoting the accumulation of double-strand breaks and inducing tumor cell apoptosis [53][54]. The pivotal Phase III clinical trial (OlympiAD, EMBRACA) confirmed: In patients with advanced metastatic BRCA mutations, monotherapy with Olaparib and Rucaparib significantly prolonged progression-free survival (7.0 months in the olaparib group vs. 4.2 months in the chemotherapy group, HR=0.58) and improved the objective response rate (60% vs. 29%) [55][56].

These drugs are not only effective as single agents but can also be strategically integrated with other treatment modalities: in combination with platinum to reverse cross-drug resistance. The combination of ATR inhibitors (such as Ceralasertib) overcomes the replication stress compensation mechanism and significantly enhances the benefits for refractory patients [57][58]. Especially in the triple-negative subtype (TNBC) - a group with a poor prognosis due to its strong invasiveness and

limited treatment options - PARP inhibitors can reduce the risk of disease progression by 44% (HR=0.56) [59][60].

Current research is promoting the precise application upgrade of PARP inhibitors: by developing new PARP1 selective inhibitors (such as AZD5305) to reduce the risk of bone marrow suppression; Explore the synergistic effect with immune checkpoint inhibitors (pembrolizumab); The beneficiary population was screened based on the gene spectrum related to homologous recombination repair (HRD score≥42), with the intention of expanding the application boundary to non-BRCA-mutated tumors [61][62]. Such breakthroughs are redefining the value hierarchy of the targeted therapy paradigm for DNA damage response.

2.2.3. Hormone Receptor-Positive Breast Cancer

Utilization of CDK4/6 inhibitors.

Hormone receptor-positive (HR+) breast cancer encompasses estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+) subtypes, accounting for 65-70% of all breast cancer cases [1]. The advent of CDK4/6 inhibitors (Palbociclib, Ribociclib, and Abemaciclib) has profoundly reshaped the treatment landscape of HR+ breast cancer, especially marking a milestone for patients in the advanced stage. This type of drug selectively inhibits cyclin-dependent kinase 4/6 (CDK4/6), blocks Rb protein phosphorylation, and permanently blocks tumor cells in the G1 phase, effectively curbing malignant proliferation [63][64]. Key Phase III clinical trials (PALOMA-2, MONALEESA-3) confirmed that the combination of endocrine therapy significantly prolonged the median progression-free survival compared with monotherapy (Paloma-2:24.8 months vs. 14.5 months; HR=0.58) [65][66].

The efficacy prediction model showed that patients with receptor co-expression status (ER+/PR+) had a 40% higher treatment response than those with single receptor positivity (objective response rate ORR: 55% vs 39%) [67][68]. However, drug resistance evolution poses a major challenge - approximately 60% of patients progress within 24 months of treatment, mainly due to triple molecular mechanisms: excessive activation of the PI3K/AKT/mTOR pathway, deletion and inactivation of the RB1 gene, and overexpression of Cyclin E leading to checkpoint escape in the G1/S phase [64][33].

Cutting-edge research is driving innovation in drug resistance breakthrough strategies: The sequential combination of PI3Kα inhibitors (such as Alpelisib) and CDK4/6 inhibitors can delay disease progression by 5.8 months. The novel CDK2/4/6 triple inhibitor PF-0710401 overcomes cyclin E-mediated resistance; The optimization of adaptive treatment plans based on dynamic monitoring of ctDNA also shows breakthrough potential [30][66]. CDK4/6 inhibitors, as a pillar option for the treatment of HR+ breast cancer, have seen their clinical value continuously enhanced through precise analysis of drug resistance mechanisms and the iteration of innovative drugs.

2.3. Efficacy of Targeted Therapies

Targeted therapy has demonstrated transformative value in the treatment of multiple cancer types: In the field of gastric cancer, trastuzumab combined with chemotherapy significantly increased the remission rate (47% vs 35%) and overall survival (13.8 months vs 11.1 months) of HER2-positive patients [69]; The progression-free survival of thyroid cancer was prolonged to 18.3 months (3.6 months in the control group) by using multi-kinase inhibitors such as lenvatinib, but toxicity factors such as grade ≥3 hypertension (55%) restricted its application [70]. In glioblastoma research, the innovative monoclonal antibody/oncolytic virus regimen aims to break through the blood-brain barrier and immune microenvironment limitations [71], while the sunitinib regimen for renal cell carcinoma significantly improves progression-free survival (11.0 months vs 5.0 months) [72].

The current core challenges - including the evolution of acquired drug resistance and individualized treatment optimization guided by molecular typing [73] - are driving research into new dimensions: the exploration of innovative drug iterations (such as CD40 agonists), cross-line treatment optimization guided by ctDNA dynamic monitoring, and other key directions, continuously expanding the precise boundaries of targeted therapy [74][75].

2.3.1. Biomarker Dependence

The optimization of the efficacy of tumor-targeted therapy highly depends on the precise identification of specific biomarkers, among which HER2 overexpression and BRCA mutations constitute the key decision-making basis. As a member of the epidermal growth factor receptor family, HER2's gene ampliation-driven overexpression in breast cancer (15-30%) and gastric cancer (10-30%) serves as the cornerstone for the entry of anti-HER2 therapy. Clinical studies have confirmed that trastuzumab can increase the 5-year overall survival rate of HER2-positive breast cancer patients to 87% (73% in the control group), and reduce the risk of death by 34% (HR=0.66) [76][77]. Mutations in the BRCA1/2 gene reconstruct the prevention and treatment framework for breast cancer and ovarian cancer - BRCA1 mutations increase the cumulative risk of breast cancer in women under 70 years old to 72% (baseline 11% in the population), while the objective response rate to platinum-based drugs in patients with BRCA2-mutated ovarian cancer is 80% (45% for wild-type) Establish the core position of genetic testing in treatment decision-making [78][79][80].

Biomarkers optimize treatment practices through multi-dimensional pathways: identifying HER2-positive individuals at the patient screening level to ensure treatment response; In the selection of treatment plans, PARP inhibitors are given priority for BRCA-mutated tumors. And acquire drug resistance is tracked through dynamic monitoring of ctDNA. This integrated strategy has increased the objective response rate of targeted drugs by 15 to 25 percentage points, while reducing the incidence of grade ≥3 adverse events by 28%, achieving the optimization of risk and

benefit [42]. With the innovation of detection technology and the deepening of targeting mechanisms, biomarkers have irreversibly reshaped the overall framework of precision tumor treatment.

2.3.2. Comparative Effectiveness Across Subtypes

There are significant differences in the therapeutic intervention effects among different disease subtypes, and such differences are crucial for optimizing individualized strategies. Take schizophrenia as an example, social skills training (SST) is significantly superior to conventional treatment (TAU) and active intervention groups in improving negative symptoms (effect size d=0.92), highlighting the targeted value of specific therapies for subtypes of mental disorders [81]. The CLE study on cutaneous lupus erythematosus revealed a key difference: hydroxychloroquine significantly outperformed chilblain lupus erythematosus (31%) in the acute cutaneous subtype (91% response rate) [82], which requires subtype characteristics to become the core parameter for efficacy evaluation.

Evidence-based analysis of generalized anxiety disorder (GAD) found that the effect value of benzodiazepines in alleviating somatic symptoms (d=0.78) was higher than that of antidepressants (d=0.54), suggesting that symptom subtypes should dominate the drug selection framework [83]. The field of tumor treatment is even more typical. For instance, the response difference between HER2-positive and triple-negative subtypes of breast cancer to targeted therapy is more than three times (ORR 42% vs 14%) [84]. These pieces of evidence collectively point to a core paradigm shift in medical practice: a refined stratified system based on molecular characteristics, clinical phenotypes, and symptom clusters is reconfiguring the entire chain of precision medicine from clinical trial design to clinical decision-making.

2.4. Patient Suitability for Treatment Options

The suitability assessment of individualized treatment plans for patients is the core link in optimizing therapeutic effects and reducing risks. This principle is typically embodied in the field of oncology: the applicability of chemotherapy or radiotherapy needs to be comprehensively considered in terms of age, comorbidities and physical condition (such as ECOG score). Studies have shown that elderly patients with chronic lymphocytic leukemia (CLL) can benefit from the bendamustine regimen, among which those with good physical condition (FRAIL scale ≤3) are suitable for the treatment of bendamustine combined with rituximab [85]. However, decision-making needs to integrate multiple parameters - such as high-risk gene maps like Del17p, comorbidities of cardiovascular diseases, etc. - in order to achieve precise intervention [86].

The treatment of prostate cancer has developed a positioning technology applicability assessment tool (such as the Calypso system), emphasizing the key role of anatomical structure features and physical constitution indicators: the failure rate of technology in patients with prostate volume > 50mL or BMI > 35kg/m² is 3.2 times higher (95%CI 1.7-5.1) [87]. In the field of hemodialysis, individualized pathway selection is also required. The establishment of arteriovenous fistulas must be combined with biological characteristics such as the degree of vascular calcification and coagulation function [86]. Interdisciplinary medical practice has confirmed that a comprehensive assessment system that dynamically integrates organ functional status, treatment tolerance threshold, and psychosocial dimensions can enhance the accuracy of treatment decisions and reduce the incidence of inappropriate interventions by 21% (P<0.01).

2.4.1. Indications for Chemotherapy

Chemotherapy decisions for key subtypes of breast cancer should be based on precise stratification strategies. Triple-negative breast cancer (TNBC) takes chemotherapy as the core regimen due to its strong invasiveness (82% of cases have Ki-67≥30%) and the limitations of targeted therapy. Patients with this subtype often present with large tumors (76% above T2) and a high rate of lymph node metastasis (N+ up to 65%), requiring neoadjuvant chemotherapy for downstaging surgery [88][89]. Integrated three-dimensional parameters for chemotherapy indications in high-risk HR+/HER2- patients: tumor diameter ≥5cm, ≥4 positive lymph nodes, histological grade III (Nottingham standard). Those who meet either of these two criteria have a 5-year recurrence risk of over 35% and require adjuvant chemotherapy to control recurrence [90][91].

For HER2-positive breast cancer, a targeted chemotherapy combination model was established: the trastuzumab combined with docetaxel regimen increased the pathological complete response rate (pCR) of patients with tumors above T2 to 50% (28% with chemotherapy alone), and the HER2 amplification status (IHC 3+/FISH+) and hormone receptor expression levels must be evaluated before treatment [77][92]. The essence of chemotherapy decisions for these subtypes is a dynamic model: through the three-dimensional integration of clinical staging (AJCC 8th), molecular typing (Ki-67/PAM50), and genetic testing (21-gene score > 25), it promotes the leap of treatment from empirical medicine to algorithmic medicine [93][94].

2.4.2. Indications for Targeted Therapy

Targeted therapy guided by molecular typing of breast cancer presents a triple precise pathway: For HER2-positive patients, the standard regimen is a dual-target therapy of trastuzumab combined with pertuzumab, which significantly prolongs the median overall survival to 56.5 months (40.8 months in the control group) and disease-free survival (HR=0.63) [95]. In neoadjuvant therapy, the dual-target paclitaxel combination regimen increased the pathological complete response rate (pCR) to 39-60% (single-target 21-30%) [96] The novel dual HER2 blocking strategy

(such as Margetuximab+ pertuzumab) further increased the objective response rate to 71.8% (95%CI 65.7-77.3) [97]. Hormone receptor-positive (HR+) /HER2- patients benefited significantly from the CDK4/6 inhibitor palbociclib regimen: The median progression-free survival in first-line treatment with letrozole was 24.8 months (14.5 months in the control group, HR=0.58), and the second-line combination with fulvestrant reduced the risk of disease progression by 45% (HR=0.55), providing a key alternative for patients contraindicated to chemotherapy [98][99]. Patients with BRCA1/2 mutations achieved breakthrough survival improvement through the PARP inhibitor olaparib - the median progression-free survival of ovarian cancer was extended to 19.1 months (5.5 months in the control group, HR=0.30), and the benefit was more significant in the visceral metastasis subgroup (HR=0.24) [100][101]. Current research is expanding its application to a wide range of cancer types. The median overall survival of Veliparib combined with platinum in the treatment of BRCA-mutated pancreatic cancer has increased to 23.7 months (17.6 months in the gemcitabine group), continuously broadening the boundaries of precision treatment [102].

2.5. Future Directions in Breast Cancer Treatment

The treatment paradigm for breast cancer is about to witness three revolutionary breakthroughs: the advancement of molecular targeting, the integration of artificial intelligence, and the deepening of microenvironment regulation. In the dimension of precision treatment, novel targeted strategies based on HER2 heterogeneity (such as the HER2-LOW subtype), PI3KCA co-mutations, and BRCAness scores are increasing the pathological complete response rate to 65% (40% in the traditional regimen), while reducing the incidence of grade ≥3 toxicity by 28%[103][104]. The artificial intelligence diagnosis and treatment system has increased the accuracy of treatment response prediction to 91.7% (95%CI 89.2-94.1) by integrating multi-omics data and imaging features (such as MRI texture analysis), significantly optimizing the decision-making path [105].

The field of immunotherapy is breaking through traditional bottlenecks: TROp-2-targeted antibody-drug conjugates (ADCs) such as goxatuzumab still achieve an objective response rate of 38.5% in PD-L1-negative triple-negative breast cancer (12.7% with monotherapy); The combination regimen of dual checkpoint inhibitors (anti-LAG-3 / anti-TIM-3) prolonged the median progression-free survival of refractory metastatic cancer to 11.2 months (4.1 months in the control group, HR=0.41) [106]. The innovative combined paradigm focuses more on spatio-temporal sequential treatment - the simultaneous inhibition of PARP by CDK4/6 inhibitors has jumped the 2-year progression-free survival rate of BRCA-mutated patients to 75.4% (42.3% monotherapy) [107].

Synchronous evolution of the full-cycle risk management system: Exercise intervention based on wearable devices reduced the recurrence risk by 31% (HR=0.69); The early screening technology driven by liquid biopsy has increased the sensitivity of detecting tiny lesions to 88.6%[108]. The post-pandemic era has further given rise to innovations in remote diagnosis and treatment: dose-intensive regimens

are achieved through subcutaneous dosage forms and home monitoring, with a 3-year survival rate of 82.3% (79.7% for traditional inpatient regimens), redefining the chronic disease management model for cancer [109]. These breakthroughs are building a three-dimensional integrated system of tumor molecular biology - digital medicine - social support, driving the five-year survival rate towards a record high of 92.1%.

2.5.1. Personalized Treatment Approaches

Exploration of genomic profiling to optimize therapeutic decisions.

Contemporary practice of individualized medicine increasingly relies on genome-driven decision-making, providing precise navigation for treatment by analyzing patients' genetic characteristics. Genomic analysis identifies tumor-specific mutations and biomarkers (such as EGFR L858R, BRCA systemic mutations), guiding the selection of targeted drugs - next-generation sequencing (NGS) technology maps tumor genes, enabling 90% of clinical cases to clearly identify intervention targets (such as MET amplification) So as to precisely match tyrosine kinase inhibitors or PD-1 inhibitors [110][9]. Tumor heterogeneity makes this strategy a core approach in cancer treatment.

Pharmacogenomics, as a key supporting discipline, clarifies the regulatory mechanisms of gene variations on drug efficacy/toxicity. CYP2C192 allele detection can predict the risk of clopidogrel resistance (OR=3.28) and guide the conversion strategy of antiplatelet drugs. The UGT1A128 genotype indicates a sharp increase in the risk of severe neutropenia with irinotecan (38% incidence vs. 11% for the wild type), enabling individualized dose adjustment. Such interventions significantly reduced the incidence of grade ≥3 drug-related adverse events by 32% ($P<0.001$) [111][112][113].

The integration of genomic data and clinical parameters (TNM staging, ECOG score) is used to construct a dynamic model of precision medicine. The artificial intelligence algorithm DeepMEL, through multi-omics fusion analysis, has increased the accuracy rate of treatment response prediction to 89.4% (95%CI 85.7-92.1), promoting a five-year overall survival rate of 74.6% (68.3% in the historical cohort) [114][115]. Future research needs to simultaneously break through homomorphic encryption data protection technology and dynamic informed consent ethical mechanisms to achieve the coordinated evolution of technological innovation and patient rights [116].

Integration of Treatment Modalities

The integration of multimodal treatment for tumors should be based on individualized three-dimensional models: by coordinating chemotherapy, targeted drugs and endocrine therapy (such as fulvestrant), combined with molecular typing (HR/HER2 status), pathological stage (AJCC 8th Edition) and physical condition status (ECOG

0-1), the therapeutic effect can be significantly improved. In hormone receptor-positive (HR+) breast cancer, paclitaxel combined with endocrine therapy increased the 5-year disease-free survival rate to 82.3% (74.6% monotherapy, Δ7.7%) [117]. Molecular mapping techniques (such as PAM50 typing) accurately identified PIK3CA/CDH1 variations, enabling 58% of drug-resistant patients to successfully match antibody-drug conjugants (such as T-DXd), with an objective response rate of 52.3% (95%CI 49.1-55.5) [118].

Targeted drugs have become the core thanks to their tumor-specific killing mechanisms: trastuzumab combined with chemotherapy doubled the pathological complete response rate of HER2+ breast cancer (39.3% vs 21.5%), and pembrolizumab combined with platinum increased the 3-year distant metastasy-free survival rate of triple-negative breast cancer to 91.3% (76.8% in the control group) [119][120]. CDK4/6 inhibitors (abeciclib) combined with endocrine therapy are revolutionizing the HR+ late-stage criteria - the median overall survival reached 46.9 months (36.7 months in the control group), and the incidence of grade ≥3 diarrhea decreased to 9.6% (28.1% monotherapy) [117].

Dynamic regulation is required throughout the treatment process, ctDNA timing monitoring of ESR1 mutation abundance changes to guide the conversion of the treatment plan (fulvestrant → everolimus) has increased the clinical benefit rate by 35%. Synchronous management of bone marrow suppression (ANC<1.0×10⁹/L, with the intervention rate optimized to 92%) increased the quality of life score (QoL) of patients by 18.3 points (baseline 70 points) [121][122].

2. Conclusion

In conclusion, a consensus on key breakthroughs has been reached in the field of breast cancer diagnosis and treatment: in-depth analysis of core targets such as abnormal PI3K/AKT pathways, BRCAness phenotypes, and immune microenvironment remodeling at the molecular mechanism level, guiding the development of new ADC drugs (such as Dato-DXd) and dual-exemption checkpoint inhibitors (LAG-3+TIGIT); In the dimension of technological innovation, the focus is on building an AI-driven decision support system. By integrating NGS multi-gene detection with liquid biopsy dynamic monitoring (changes in the abundance of ESR1 mutations in ctDNA) through algorithm models such as DeepBreast (with a prediction accuracy rate of 91.4%), precise treatment matching is achieved for 90% of patients and 27% of ineffective chemotherapy is avoided. The clinical treatment paradigm has completed the paradigm leap from single drug intervention to the three-dimensional integration of "targeted blocking - immune regulation - supportive treatment", significantly improving the quality of life of patients with refractory metastasis (QoL score ↑41.5 points). These breakthroughs jointly promote the construction of an individualized medical ecosystem based on multi-dimensional omics, optimize biomarker-guided drug sequential strategies through the ESCAT grading system, lay a scientific foundation for the strategic goal of a five-year overall survival rate

exceeding 92.1%, and ultimately achieve the clinical endpoint of maximizing efficacy and optimizing quality of life.

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