

Research Article

Research Progress of Traditional Chinese Medicine in HER-2 Positive Invasive Breast Cancer

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Abstract

Objective: This study reviews the research progress, mechanisms of action, and clinical value of Traditional Chinese Medicine (TCM) in treating HER2-positive breast cancer, while exploring future research directions.

Methods: A systematic literature review was conducted through databases including CNKI, Wanfang, VIP, and PubMed, with a focus on TCM's immune regulation, drug resistance reversal, cardioprotective mechanisms, and clinical combination applications.

Results: TCM exerts synergistic effects through multiple mechanisms: Mechanistically, it modulates immune microenvironment parameters such as IL-17 and PD-1/PD-L1, controls PI3K/AKT/mTOR signaling pathways to reverse drug resistance, and improves cardiac function by enhancing left ventricular ejection fraction (LVEF) and cardiac troponin I (cTnI) levels. Clinically, TCM combined with targeted therapies enhances survival rates, reduces treatment-related adverse reactions, and improves quality of life.

Conclusion: TCM demonstrates unique advantages in HER2-positive breast cancer treatment through reduced toxicity and enhanced efficacy while improving quality of life. However, further mechanistic studies and high-quality clinical trials are required to provide higher-level evidence-based medical support.

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Keywords: Cardioprotective; HER-2-Positive Breast Cancer; Immune Microenvironment; Multidrug Resistance; Synergistic Therapy; Traditional Chinese medicine

Domestic and International Research Status

Mechanism of Traditional Chinese Medicine in HER-2 positive breast cancer

Traditional Chinese Medicine (TCM) Regulates Immune Environment to Control HER-2-positive Breast Cancer Development. TCM demonstrates unique advantages in optimizing the tumor immune environment. Li Feifei et al., found that the herbal formula Wenjing Tang enhances immune function by regulating IL-17 and PD-1/PD-L1 secretion, while addressing immune microenvironment imbalance in cancer patients. Wu Xueqing et al., reported that postoperative interventions increased CD4⁺/CD8⁺ T cell ratios in mouse spleens, promoting IL-2, IL-12, and IFN- γ secretion to boost anti-tumor immunity [1]. Zhou Siying et al., revealed that TCM formulas modulate TNF- α and IL-2 cytokines to exhibit antitumor effects: TNF- α promotes inflammatory cell infiltration in tumor areas, while IL-2 activates natural killer cells to enhance immune function [2]. Shao Shijun et al., further demonstrated that the TCM formula "Ruchang Qixie" significantly improved disease-free survival rates in HER-2-positive breast cancer patients, likely due to its immune regulation effects [3]. These studies collectively confirm that traditional TCM modulates tumor immune microenvironments through multi-target pathways, providing novel therapeutic strategies for HER-2-positive breast cancer progression control.

The Efficacy of Traditional Chinese Medicine Formulations in Reversing Multidrug Resistance in HER-2-positive Breast Cancer. Traditional Chinese medicine formulations demonstrate significant potential in combating multidrug resistance in HER-2-positive breast cancer. Studies indicate that these formulations can effectively reverse tumor resistance by modulating signaling pathways in tumor cells, inhibiting chemoreceptor effector proteins (CPEPs), and inducing apoptosis. According to Chen Qianjun et al., TCM formulations can reverse multidrug resistance by regulating cytokine expression such as TNF- α and IL-2 [2]. Li Feifei et al., further noted that combining TCM formulations with trastuzumab using the therapeutic principle of "strengthening vital energy, eliminating pathogens, invigorating qi, activating blood circulation, and resolving stasis" significantly reduces Carcinoembryonic Antigen (CEA) and carbohydrate antigen 153 (CA153) levels in HER-2-positive breast cancer patients [1]. TCM formulations primarily inhibit cancer cell growth and metastasis by regulating signaling pathways including PI3K/AKT/mTOR and MAPK. Chen Rong (2009) demonstrated that TCM formulations enhance chemotherapy response by modulating HER-2 signaling pathway molecules [4]. Additionally, TCM formulations enhance immune responses by adjusting tumor microenvironmental immune cell functions. Wang Min et al., revealed that TCM formulations can reverse

tumor cell resistance to targeted therapies by regulating immunosuppressive factors in the tumor microenvironment [5].

Traditional Chinese medicine's protective effects on cardiac function in HER-2-positive Breast Cancer Patients Targeted therapies against HER-2 often cause cardiotoxicity, but traditional Chinese medicine offers multiple approaches to mitigate such damage. According to Shi Wenxian's research, Xiaoyao San and Kaixin San demonstrate protective effects against heart damage caused by trastuzumab. Studies indicate these medications significantly improve Left Ventricular Ejection Fraction (LVEF) and help alleviate tumor-related depressive symptoms [1]. Zhang Yang et al. 's study shows that Jiao-wei Shengmai Yin enhances patients' tolerance to heart damage induced by Herceptin and reduces the decline in LVEF [1]. He Nana et al.'s research reveals that Tongyang Qiuju Traditional Chinese Medicine lowers cardiac troponin (cTnI), blood rheology parameters, and Human Heart Fatty Acid-Binding Protein (H-FABP) levels, thereby maintaining normal cardiac function [1]. Additionally, combining traditional Chinese medicine formulations with trastuzumab reduces side effects such as skin itching, gastrointestinal discomfort, and liver function impairment [1].

Clinical study of combined targeted therapy of HER-2 positive breast cancer with Traditional Chinese medicine

Combined use of Chinese herbal compound and trastuzumab improves the survival status of HER-2 positive breast cancer patients: The combination of these approaches has demonstrated significant efficacy in improving patients' quality of life. According to Li Feifei et al., the combination of traditional Chinese medicine formulas with trastuzumab can significantly reduce CEA and CA153 levels while effectively minimizing adverse reactions [1]. Zhang Qi et al., found that this combined strategy enhances immune function by regulating cytokines such as IL-2 and IL-12, thereby extending progression-free survival (PFS) and overall survival (OS) [6]. Shao Shijun et al., revealed that combining "Ruchang Houxiang" with trastuzumab markedly improves disease-free survival rates [3]. Wang Zhaobu et al., demonstrated that traditional Chinese medicine formulas inhibit HER-2 signaling pathways, enhancing tumor cells' response to targeted therapies [7].

Effect of Traditional Chinese medicine in alleviating adverse reactions caused by targeted therapy: Clinical trial results demonstrate that traditional Chinese medicine (TCM) significantly reduces adverse reactions caused by targeted therapy. Studies indicate that TCM compound formulas effectively alleviate skin itching, gastrointestinal discomfort, and liver function impairment induced by trastuzumab [1]. The Qizhudi Ling Compound shows remarkable efficacy in relieving symptoms such as fatigue and mental exhaustion, while also reducing the incidence of bone marrow suppression and digestive system disorders [1]. Postoperative breast cancer patients may experience symptoms like lower back and knee soreness and extreme fatigue, which can be alleviated through appropriate interventions [1]. Huangqi Zhishi Decoction helps maintain immune system function and improves patients' quality of life [1].

The key role of TCM in adjuvant therapy for HER-2 positive breast cancer: The application of traditional Chinese medicine (TCM) in adjuvant therapy has gained increasing recognition. Researchers such as Zhang Qi et al. (2024) demonstrated that combining TCM formulations with neoadjuvant chemotherapy significantly improves pathological Complete Response Rate (pCR) [6]. Wang

Chao-bin et al., highlighted that integrating TCM with endocrine therapy and targeted treatment may exempt HR-positive/HER2-positive patients from chemotherapy [8]. According to Liu Jian-lan et al., TCM treatment markedly enhances therapeutic outcomes [9]. Xin Ling et al.'s 2024 [10] study further revealed that TCM combination therapy not only elevates pCR rates but also effectively reduces treatment-related adverse reactions [11].

Improvement of quality of life in HER-2 positive breast cancer patients with TCM

The Impact of Traditional Chinese Medicine (TCM) on Postoperative HER-2-positive Breast Cancer Patients: TCM has demonstrated significant advantages in reducing postoperative complications. According to Yang Fan et al., the combined application of warming yang and diuresis formulas with pressure drainage significantly reduces postoperative subcutaneous fluid accumulation [12]. Lü Su-jun et al., found that using blood-activating and meridian-connecting anti-edema herbal formulas shows remarkable efficacy in treating postoperative upper limb edema [5].

Traditional Chinese Medicine (TCM) in Managing Chemotherapy-Related Symptoms of HER-2-positive Breast Cancer TCM demonstrates significant efficacy in alleviating chemotherapy-induced symptoms. Medicinal formulations such as Qizhudi Ling Compound and Postoperative Formula for Breast Cancer can effectively reduce fatigue, bone marrow suppression, and gastrointestinal discomfort [1]. By enhancing qi circulation, strengthening spleen function, and regulating gastric motility, TCM therapies help relieve postoperative appetite loss and nausea/vomiting [5]. Additionally, Yangzheng Xiaojie Capsule provides preventive support against chemotherapy-associated digestive side effects [5].

The Impact of Traditional Chinese Medicine on Mental Health in HER-2-positive Breast Cancer Patients Traditional Chinese medicine demonstrates unique advantages in improving patients' mental health. The combined use of Xiaoyao San and Kaixin San effectively alleviates tumor-related depressive symptoms [1]. A comprehensive syndrome-specific strategy incorporating TCM diagnosis and treatment can significantly enhance patients' psychological well-being and quality of life. According to Zheng Xiaojun et al., [13] TCM shows remarkable efficacy in reducing psychological distress such as anxiety and depression [14,15].

Brief Review

Advantages and limitations of TCM in HER-2 positive breast cancer

Traditional Chinese Medicine (TCM) demonstrates unique advantages in multi-target regulation, particularly in enhancing immune function, reversing drug tolerance, protecting the heart, and improving quality of life. Current research faces several constraints: most mechanistic studies focus on single targets with insufficient comprehensive analysis. Clinical trials often have small sample sizes and lack support from multicenter large-scale Randomized Controlled Trials (RCTs). The dosage, duration, and specific mechanisms of combination therapies remain unclear; further research is needed to evaluate the long-term efficacy and safety of neoadjuvant therapies.

Discussion on the synergistic mechanism of combined targeted therapy in TCM

Breakthroughs have been made in studying the synergistic mechanisms between traditional Chinese and Western medicine, primarily manifested in enhanced cancer treatment efficacy, improved immune microenvironment, and reduced side effects. However, several limitations remain: specific molecular mechanisms have not been fully elucidated; the quality of clinical research evidence is suboptimal; and standardized treatment protocols for comprehensive therapies have yet to be established.

Future research direction of TCM in HER-2 positive breast cancer treatment

Future research should focus on conducting comprehensive and systematic investigations into the synergistic mechanisms of multiple therapeutic targets; implementing large-scale, multi-center randomized controlled trials with thorough evaluation; developing optimized treatment strategies that integrate traditional Chinese medicine with targeted therapies, including dosage optimization and treatment duration planning. Additionally, it is crucial to investigate the potential efficacy and long-term effects of TCM as an adjuvant therapy before surgery.

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