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Original Paper

The Efficacy of the Dual-targeted Drug Combination Regimen Combined with TCb in Neoadjuvant Chemotherapy for HER2-Positive Breast Cancer and Its Impact on Tumor Markers

Wenbin Chen[1], Peizhen Gao[1], Yankai Xing[2], Ximin Yuan[1], Junran Wang[1], Minghai Gong[1*]

[1] College of Medicine, Tarim University, Alar, Xinjiang Uygur Autonomous Region 843300

[2] Henan University of Chinese Medicine, Zhengzhou, Henan Province 450046

[*] Corresponding author, Minghai Gong

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Abstract

Objective: To investigate the clinical efficacy of the trastuzumab plus pertuzumab (biclusal targeted therapy) combined with the TCb regimen (docetaxel + carboplatin) in neoadjuvant chemotherapy for HER2-positive breast cancer, as well as its impact on serum tumor markers. Methods: A total of 112 HER2-positive breast cancer patients admitted to our hospital between June 2023 and December 2025 were enrolled and randomly assigned into two groups using a random number table: the observation group (n = 56) and the control group (n = 56). The control group received the TCb chemotherapy regimen, while the observation group received the TCb regimen combined with trastuzumab and pertuzumab as dual-targeted therapy; both groups underwent a total of 6 cycles of treatment. The objective response rate (ORR) and pathological complete response (pCR) rate were compared between the two groups. Serum levels of carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and carbohydrate antigen 153 (CA153) were measured before and after treatment, and the incidence of adverse reactions was recorded. Results: The observation group exhibited a higher ORR and pCR rate compared to the control group. After treatment, the serum levels of CEA, CA125, and CA153 in the observation group were lower than those in the control group (P <0.05). There was no statistically significant difference in the incidence of adverse reactions between the two groups (P> 0.05). Conclusion: The use of the dual-targeted therapy combined with the TCb regimen can enhance the efficacy of neoadjuvant chemotherapy in HER2-positive breast cancer, reduce serum tumor marker levels, and does not significantly increase the incidence of adverse reactions.

Keywords

HER2-positive breast cancer, dual-targeted therapy, neoadjuvant chemotherapy, tumor markers, trastuzumab; pertuzumab

1. Introduction

Breast cancer currently accounts for the highest proportion of malignancies worldwide; the HER2-positive subtype is generally more aggressive, characterized by rapid disease progression and a relatively high risk of long-term recurrence and distant metastasis. Due to the aberrantly high expression of HER2 in the tumor microenvironment, it continuously activates multiple downstream signaling pathways in tumor cells, persistently promotes their proliferation and differentiation, and induces angiogenesis—factors that collectively contribute to the poorer overall prognosis in patients with this subtype of breast cancer [1-2]. The clinical introduction of trastuzumab has revolutionized the traditional treatment approaches for HER2-positive breast cancer, leading to significant improvements in both survival duration and long-term prognosis for these patients [3]. The dual-targeted therapy regimen combining trastuzumab and pertuzumab, developed building upon the concept of single-targeted agents, enables more comprehensive blockade of signaling pathways and exerts a stronger antitumor effect; this approach is now increasingly being incorporated into neoadjuvant treatment strategies for high-risk HER2-positive breast cancer [4-5]. The administration of neoadjuvant chemotherapy can effectively decrease the tumor size, reduce the clinical tumor stage and enhance the possibility of performing a breast conserving operation; besides, the postoperative pathological reaction can be used as a reliable standard for choosing the subsequent adjuvant treatment regimen. In the conventional chemotherapy alone regimens, the incidence of pathological complete response (pCR) is relatively low; thus, the evidence demonstrating the effectiveness of dual-targeted drug combination in conjunction with platinum-based chemotherapy regimens still needs to be verified and expanded by further clinical trials [6]. Based on the present clinical situation, our study intends to carry out a comparative observational study on HER2-positive breast cancer patients to assess the clinical effect of dual-targeted therapy in combination with TCb during the neoadjuvant treatment, and to investigate its influence on the serum tumor marker expressions in these patients. The results will provide a useful basis for improving the neoadjuvant treatment methods for patients with similar conditions in clinical practice.

2. Materials and Methods

2.1 General Information

A total of 112 HER2-positive breast cancer patients, all admitted to our hospital between September 2023 and December 2025, were enrolled in this study. The patients were randomly assigned into two groups using a random number table: 56 patients in each group (Observation Group and Control Group). The baseline characteristics of the two groups were comparable ($P > 0.05$). See Table 1.

Table 1. Comparison of Baseline Characteristics between $\bar{x} \pm s$ $\bar{x} \pm s$ the Two Groups [n, (%,)]

group	N	Age (years)	Clinical staging (Stage II/Stage III)	Hormone receptor status (positive/negative)	Ki67(< 30%/≥30%)
observation group	56	49.3±8.7	34/22	30/26	24/32
control group	56	48.7±9.2	36/20	28/28	26/30
statistic		0.354	0.152	0.143	0.144
P		0.723	0.696	0.705	0.703

Inclusion criteria: (1) Invasive breast cancer confirmed by pathological diagnosis via hollow-core needle biopsy; (2) HER2 positivity confirmed by immunohistochemistry (IHC 3+ or FISH-positive); (3) Clinical stage II-III (AJCC 8th edition); (4) Age ≥ 18 years; (5) Eastern Cooperative Oncology Group (ECOG) performance status score of 0-1; (6) Left ventricular ejection fraction ≥ 55%; (7) No contraindications to chemotherapy based on major organ function tests.

Exclusion criteria: (1) Prior receipt of anti-HER2 targeted therapy or chemotherapy; (2) Bilateral breast cancer or coexisting other malignant tumors; (3) Pregnant or lactating women; (4) Severe cardiovascular or cerebrovascular diseases or coagulation disorders; (5) Presence of distant metastases; (6) History of hypersensitivity to the investigational drug.

2.2 Methodology

Control group: The TCb chemotherapy regimen was selected as the pharmacological treatment option for neoadjuvant therapy; the selection of docetaxel and carboplatin was identical. Docetaxel (Guangdong Xinghao Pharmaceutical Co., Ltd., H20198003,2 mL: 80 mg) was administered at a dose calculated as 75 mg/m², given via intravenous infusion on the first day of each treatment cycle; Carboplatin (Sichuan Baili Pharmaceutical Co., Ltd., H20249713,15 mL: 150 mg) was administered at a dose determined based on the area under the curve (AUC) set to 6, given via intravenous infusion on the first day of each cycle. In this study, each treatment cycle was defined as lasting 21 days, and all enrolled control cases completed a full course of six treatment cycles of chemotherapy.

The observation group received dual-targeted therapy in addition to the standard treatment regimen: Trastuzumab (Shanghai Fosun Ruilin Biotechnology Co., Ltd., S20200019,150 mg/vial): initial intravenous infusion of 8 mg/kg, followed by weekly administration (6 mg/kg) on day 1; Pertuzumab (Shanghai Fosun Hanlin Biopharmaceutical Co., Ltd., S20260034,420 mg (14 mL)/vial): initial intravenous infusion of 840 mg, followed by weekly administration (420 mg) on day 1; each treatment cycle lasted 21 days, with a total of 6 cycles. Prior to chemotherapy, all patients received dexamethasone pretreatment to prevent allergic reactions, and symptomatic supportive care—including antiemetic, platelet-raising, or granulocyte-raising therapies—was administered selectively based on disease status. During treatment, routine blood counts, liver and kidney function tests, and electrocardiogram (ECG) findings were closely monitored; if grade III or higher hematologic or non-hematologic toxicity occurred,

the drug dosage was adjusted accordingly. All patients underwent radical mastectomy or breast-conserving surgery within 2-4 weeks after completion of neoadjuvant chemotherapy.

2.3 Observation Measures

(1) Short-term efficacy: After completion of six treatment cycles, the objective response rate (ORR) - including complete response (CR) and partial response (PR) - was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST 1.1). Postoperative pathological specimens were evaluated for pathological complete response (pCR) using the Miller-Payne grading system; pCR was defined as the absence of residual invasive carcinoma in both the primary breast lesion and regional lymph nodes (ypT0/Tis ypN0).

(2) Serum tumor markers: 5 mL of fasting morning peripheral venous blood was collected before treatment and after 6 treatment cycles (preoperatively). After centrifugation to isolate serum, the levels of carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and carbohydrate antigen 153 (CA153) were measured using electrochemiluminescence immunoassay. The normal reference ranges are: CEA <5.0 ng/mL, CA125 <35 U/mL, and CA153 <31.3 U/mL.

(3) Adverse reactions: The occurrence of adverse reactions during treatment—including myelosuppression, gastrointestinal reactions, hepatic impairment, cardiac toxicity, etc.—was assessed in accordance with the Common Terminology Criteria for Adverse Events (CTCAE 5.0) issued by the National Cancer Institute.

2.4 Statistical Methods

Statistical analysis was performed using SPSS 25 software; categorical and continuous variables were expressed as mean ± standard deviation or as percentages (%), respectively. Differences between the two groups were compared using the t-test, chi-square test, or Fisher's exact probability test. ($P < 0.05$)

3. Results

3.1 Comparison of Short-term Efficacy between the Two Groups

The observed group achieved an ORR of 78.57%, comprising 18 cases of CR and 26 cases of PR; the control group achieved an ORR of 58.93%, comprising 10 cases of CR and 23 cases of PR; the difference in ORR between the two groups was statistically significant ($P < 0.05$). The pCR rate in the observed group was higher than that in the control group ($P < 0.05$). See Table 2.

Table 2. Comparison of short-term efficacy between the two groups [n, (%)]

group	N	CR	PR	SD	PD	ORR	pCR
observation group	56	18(32.14)	26(46.43)	9(16.07)	3(5.36)	44(78.57)	31(55.36)
control group	56	10(17.86)	23(41.07)	15(26.79)	8(14.29)	33(58.93)	19(33.93)
x^2						5.028	5.202
P						0.024	0.022

3.2 Comparison of Serum Tumor Marker Levels before and after Treatment between the Two Groups

Before treatment, the serum levels of CEA, CA125, and CA153 were similar between the two groups (P> 0.05). After six cycles of treatment, the levels of all these markers decreased compared to baseline; in the observation group, all marker levels were lower than those in the control group (P <0.05). See Table 3.

Table 3. Comparison of Serum Tumor Marker Levels before and after Treatment between the Two Groups [n，($\bar{x} \pm s$)]

group	N	CEA(ng/mL)		CA125(U/mL)		CA153(U/mL)	
		pretherapy	post-treatment	pretherapy	post-treatment	pretherapy	post-treatment
observation group	56	11.3±4.7	3.5±1.6*	42.7±15.2	18.4±7.3*	38.5±13.8	15.3±5.9*
control group	56	10.8±5.1	5.8±2.4*#	41.9±16.4	26.7±9.6*#	37.6±14.5	23.5±8.2*#
t		0.539	5.967	0.267	5.150	0.336	6.074
P		0.590	< 0.001	0.789	< 0.001	0.737	< 0.001

Note. Compared to the pre-treatment value in the same group, *P<0.05; compared to the post-treatment value in the control group, #P<0.05.

3.3 Comparison of Adverse Reactions between the Two Groups

The primary adverse reactions in both groups included bone marrow suppression, gastrointestinal disturbances, hepatic impairment, and cardiac toxicity; these reactions were predominantly grade I-II and could be alleviated with symptomatic treatment. There was no statistically significant difference in the incidence of adverse reactions between the two groups (P> 0.05). No treatment-related mortality events occurred in either group. See Table 4.

Table 4. Comparison of Adverse Reactions between the Two Groups [n, (%)]

untoward effect	Observation group (n=56)	Control group (n=56)	χ^2price	Pprice
neutropenia	38(67.86)	35(62.50)	0.038	0.844
thrombocytopenia	25(44.64)	21(37.50)	0.590	0.442
anemia	22(39.29)	19(33.93)	0.346	0.556
Nausea/Vomiting	30(53.57)	28(50.00)	0.143	0.705
diarrhoea	17(30.36)	11(19.64)	1.714	0.190
Hepatic dysfunction	14(25.00)	12(21.43)	0.198	0.656
Cardiotoxicity	3(5.36)	2(3.57)	0.209	0.647

4. Discussion

Patients who are treated with single-targeted drugs may show resistance or acquired resistance during the treatment process, thus the therapeutic effect is not very satisfactory. The target of pertuzumab is different from that of trastuzumab - pertuzumab binds to different epitopes of the HER2 receptor. When used in combination with trastuzumab, this dual-targeted method can inhibit the formation of both homodimers and heterodimers of HER2 complexes, which can enhance the inhibition of tumor cells [7]. Although many clinical trials, such as those in NeoSphere and TRYPHAENA, have indicated the benefits of dual-targeted combined chemotherapy regimens in neoadjuvant therapy, the clinical efficacy and safety profile of various chemotherapy drug combinations still need to be further verified by more real-world clinical data.

This research showed through statistical analysis that, after treatment with the dual-targeted TCb regimen, the objective response rate (ORR) in the observation group was 78.57%, and the pathological complete response (pCR) rate was 55.36%. Both efficacy indicators were significantly higher than those in the control group which received only the corresponding chemotherapy regimen. These results provide sufficient evidence that the addition of trastuzumab and pertuzumab to a taxane-and platinum-based chemotherapy regimen can effectively improve the short-term efficacy of neoadjuvant therapy in HER2-positive breast cancer patients. According to previous clinical studies, the pCR rate with the TCbHP regimen usually varies from 65% to 76%; however, the efficacy data in different studies may differ somewhat. This variation is mainly due to factors such as the tumor stage of the enrolled patients, hormone receptor expression status, and the sample size. In this group, the pCR rate obtained by the dual-targeted therapy was slightly lower than the previously reported values in literatures. The analysis of the enrolled patients' baseline characteristics indicated that 39.29% of the patients had stage III disease, and more than half of the cases were hormone receptor positive, suggesting a generally more advanced disease condition at the beginning. Previous clinical data have shown that hormone receptor positive HER2 positive breast cancer patients usually have lower sensitivity to targeted therapy compared to hormone receptor negative patients, which may be the main reason for the low pCR rate observed in this study [8-9].

Serological tumor marker assays are easy to operate and can give a clear reflection of the treatment result in breast cancer patients; they are also applicable in long-term follow-up to detect the risk of recurrence and metastasis, therefore being a very useful evaluation way in the present clinical diagnosis and management of breast tumors. Among these markers, CEA, CA125 and CA153 are commonly used in the screening and evaluating the effectiveness of breast cancer, because their expressions can accurately show the variations of the tumor burden in the body. The follow-up test results of our study showed that after receiving stage-specific neoadjuvant therapy, the serum concentrations of CEA, CA125 and CA153 were reduced in both patient groups to different extents; however, in the group which received dual-targeted combined chemotherapy, the decrease of these markers was more obvious and the overall serum marker levels were maintained at a lower level after treatment completion. The change pattern of these

markers indicates that the dual-targeted combined chemotherapy has a more significant inhibitory effect on the proliferation of breast cancer cells. The two targeted agents can block the HER2 signal pathway simultaneously and non-overlappingly, thus synergistically enhancing the body's immune ability to eliminate tumor cells. Some previous clinical trials have proved that this dual-targeted intervention can improve the presentation of tumor cell surface antigens and promote the infiltration and recruitment of T lymphocytes at the lesion site, which may further enhance the body's inherent immune reaction against tumors. This phenomenon is an important internal reason for the marked reduction of serum tumor marker levels and the improved overall anticancer effect of this treatment method [10].

The result of the statistical investigation on the safety of this treatment showed that the different types of adverse reactions occurred in the same way in the two patient groups; the most common side effects were bone marrow suppression and gastrointestinal discomfort during the study. Moreover, no severe side effects were found in any of the enrolled patients and the treatment period was not interrupted or terminated because of intolerable toxic reactions. The incidence rate of diarrhea was slightly higher in the observation group; however, these symptoms were mild to moderate and could be well controlled by routine symptomatic treatment and nutritional support measures, which did not affect the final treatment effect. As for the possible cardiotoxicity caused by the clinical application of dual-targeted therapies, there was no significant difference in the initial data of the two groups. This was partly because of the strict selection of patients' baseline cardiac functions at the beginning of the study, selecting only those with normal cardiac functions; it was also because the chemotherapy regimen TCb used in this study did not contain anthracycline-based drugs, thus avoiding the risk of additive cardiotoxicity from adding such drugs [11-12]. The combination of dual-targeted therapies with the TCb chemotherapy regimen can improve the overall efficiency of new adjuvant therapy for HER2-positive breast cancer while maintaining the treatment safety and satisfactory patient tolerance; the therapeutic benefits are reasonable.

In summary, the combination of a dual-targeted drug regimen with TCb can improve the effect of neoadjuvant chemotherapy for HER2-positive breast cancer, decrease the serum tumor marker levels, and does not increase the incidence of side effects significantly. This present study is a single-centre, unblinded trial with a limited number of samples; hence, further research is needed to increase the sample size and prolong the follow-up time to confirm its influence on long-term survival.

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