BMC Women's Health

RESEARCH

Open Access

Intensive treatment of triple negative breast cancer with residual positive axillary lymph node after neoadjuvant chemotherapy

Xing Wang[1], Yingjian He[1], Jinfeng Li[1], Tianfeng Wang[1], Zhaoqing Fan[1*] and Tao Ouyang[1*]

Abstract

Background Neoadjuvant chemotherapy (NAC) with anthracycline sequential paclitaxel is the standard regimen for triple negative breast cancer (TNBC), while TNBC with residual positive axillary lymph node after standard NAC indicates poor prognosis. There is no evidence that vinorelbine alone can be used as an adjuvant intensive therapy for such patients at present.

Methods We recruited TNBC patients with clinical stage of T1-4/N1-3/M0, who received NAC with 8 cycles of anthracycline sequential paclitaxel and had residual tumor in axillary lymph node after surgery. The patients were randomly divided into adjuvant intensive treatment group (Group A) and control group (Group B). The patients in group A received vinorelbine at a dose of 25 mg/m^2 on days 1/8 of a 21-day cycle with four planned cycles, while the control group received no therapy. Stratified according to the Miller-Payne system of the primary lesion (G1-2/G3-5). The endpoints included distant disease-free survival (DDFS), recurrence-free survival (RFS), overall survival (OS), and safety.

Results A total of 22 eligible patients were enrolled in this study, the 3-year DDFS and RFS rates in the group A were significantly higher than those in group B (90.0% vs. 42.4%, $p=0.022$, both) at a median follow-up of 36 months. All patients in the group A completed the scheme in full dose, and no grade 3/4 adverse event occurred.

Conclusions TNBC patients with residual positive axillary lymph nodes after NAC of anthracycline sequential paclitaxel could benefit from adjuvant intensive therapy of vinorelbine with a good safety.

Trail registration The study was registered on the Clinical Trial registry website (https://register.clinicaltrials.gov, NCT03270007) (Registration Date: 08/30/2017).

Keywords Adjuvant intensive therapy, Triple-negative breast cancer, Neoadjuvant chemotherapy, Residual positive axillary lymph nodes, Miller-Payne system

*Correspondence:
Zhaoqing Fan
zhqfan@bjmu.edu.cn
Tao Ouyang
breastcenter666@163.com
[1]Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Breast Cancer Prevention and Treatment Center, Peking University Cancer Hospital & Institute, Beijing 100142, China

Background

Breast cancer is the most frequently occurring malignant tumor in females worldwide [1, 2]. Among the many subtypes of breast cancer, triple-negative breast cancer (TNBC) is particularly challenging to treat due to its lack of expression of certain receptors that are typically targeted in other breast cancer subtypes. TNBC is a subtype of breast cancer detected using immunohistochemistry and is characterized by <1% expression of estrogen receptor (ER) and progesterone receptor (PR) and a negative expression of human epidermal growth factor receptor-2 (HER-2). TNBC accounts for approximately 12–17% of breast cancer cases and has a poorer prognosis [3, 4], making it a particularly urgent area of research. Effective treatment options for TNBC are therefore desperately needed, and ongoing research efforts aim to identify new strategies for combating this deadly disease.

One of the standard systemic treatment options for TNBC is anthracycline followed by paclitaxel NAC. In fact, PCR has an impact on triple negative and HER2, but not on luminal tumors [5]. A previous study [6] revealed that, in locally advanced breast cancer (LABC) with axillary lymph node metastasis, there is a statistically significant difference in the 3-year DDFS rate between patients who achieve complete remission in the axillary lymph nodes after NAC and those with cancer residual (91.7% vs. 78.8%, $P=0.016$, HR=2.17). In patients with hormone receptor-negative and residual lymph node cancer who did not receive postoperative adjuvant therapy, the risk of distant metastasis and death increased by 4.256 times (95% confidence interval [CI]: 1.14–24.17, $P=0.033$) and 6.478 times (95% CI: 1.58–35.30, $P=0.011$), respectively. These results are consistent with those of the CREATE-X study [8].

Vinorelbine is a classic anti-microtubule cytotoxic drug. Previous studies have reported that vinorelbine, as a salvage treatment for metastatic breast cancer, can prolong the time to progression by 4.5 to 5.8 months and can increase the objective response rate by approximately 36–41% [9, 10]. At present, there is no study on vinorelbine monotherapy as the first-line adjuvant therapy for early breast cancer. Thus, a single-center, randomized phase 3 clinical trial (BCP-19) was designed to evaluate the safety and efficacy of vinorelbine as an adjuvant intensified therapy for lymph node-positive TNBC patients with residual cancer in the lymph nodes after NAC with anthracycline followed by paclitaxel.

Methods

Patients

Patients with primary invasive breast cancer who were pathologically confirmed to be negative for hormone receptors (ER<1%, PR<1%) and HER-2 (−/1+or 2+without amplification detected via FISH) were recruited in this study. The clinical stage of the tumor in these patients was T1-4/N1-3/M0. The patients received eight cycles of NAC with anthracycline followed by paclitaxel before surgery. After NAC, residual cancer in the ipsilateral axillary lymph node was pathologically confirmed, regardless of residual cancer in the primary tumor. The inclusion criteria were as follows: patients aged 18–66 years; females; those able to tolerate chemotherapy; and those without a history of other tumors, severe cardiovascular disease, uncontrolled infection, and contraindications to radiotherapy and chemotherapy. In addition, the patients should have normal laboratory results for the blood, cardiac, liver, and kidney function tests.

Experimental design

Patients who satisfied the inclusion criteria were randomly divided into the adjuvant intensive treatment group (group A) or the control group (group B) after signing the informed consent form. Since the sensitivity of the primary tumors to chemotherapy may lead to differences in prognosis, random enrollment should be stratified according to the pathological Miller–Payne classification of primary tumors. Patients in group A received four cycles of intensive adjuvant chemotherapy, with vinorelbine tartrate as the main chemotherapy drug with a dose of 25 mg/m^2 administered intravenously (IV) D1, D8 Q21. Since extravasation of vinorelbine during infusion may lead to severe local tissue necrosis or thrombophlebitis [11], a central venous catheter was inserted for group A prior to adjuvant chemotherapy. After four cycles of chemotherapy, all patients received radiotherapy and started follow-up. In addition, the control group received the previous treatment plan without any adjuvant chemotherapy, followed by postoperative radiotherapy and follow-up. In this study, the Miller–Payne grading system was used for the pathological evaluation of the primary lesion [12], which was divided into two layers: G1/2 indicates that the primary lesion has no obvious regression, and G3/4/5 indicates that the primary lesion has significantly regressed (Fig. 1). This study was funded by Jiangsu Haosen Pharmaceutical Group Co., Ltd., and vinorelbine for injection (Gaynor) test drug and subclavian puncture catheter materials were provided free of charge. The sponsors were not involved in any matters related to the trial design, data collection and analysis, or interpretation of results.

Study endpoints

The primary endpoint of this study was the DDFS, which was the time from randomization to distant organ metastasis or death from any cause. The secondary endpoints included RFS and OS. RFS was defined as the time from randomization to recurrence, metastasis, second primary

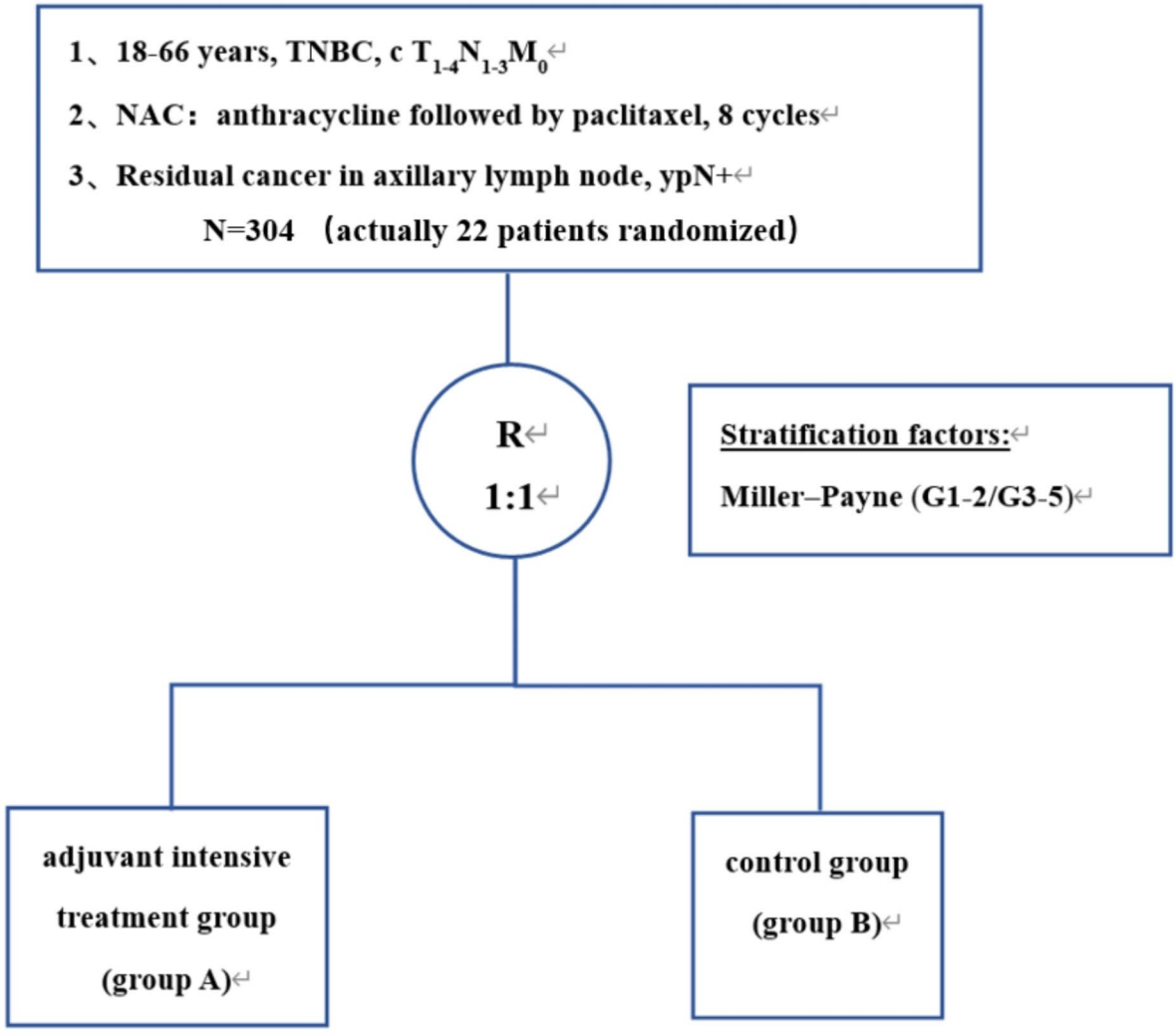

Fig. 1 Flowchart of patient selection in this study

cancer, or death from any cause. OS was defined as the time from randomization to death from any cause. To evaluate the clinical safety of the treatment in the study, NCI-CTC AE version 4.0 was used. Regardless of whether an adverse event had a causal relationship with the trial drug, this study recorded all adverse events in the original records and transferred them to the case report form. Adverse events also included the increase in the number and severity of illnesses that were present before the start of the study. The specific record content included the description of adverse events, occurrence time, termination time, degree and frequency of attack, and whether treatment was required. If treatment was required, the treatment plan provided was recorded. The investigator was responsible for judging whether the adverse event was related to the trial.

Statistical analysis

This trial was a single-center, prospective, randomized clinical trial, and the primary endpoint was the DDFS. According to the previous data of our center, the 5-year DDFS of the group without adjuvant chemotherapy was 78.6%, and the 5-year DDFS of the adjuvant chemotherapy group was expected to increase to 90.0%. The time of enrollment and follow-up of this study were expected to be 3 and 5 years, respectively. The minimum required number of patients in each group was 138 with the power of 0.85 and α of 0.05. Considering that the withdrawal rate was not higher than 10%, 152 cases were needed for each group. A total of 304 eligible cases (at least 55 DDFS events) were required for the study. Statistical analysis was performed using SPSS 22.0 software. All statistical tests were two-sided, and statistical significance was set at a P value of <0.05. For measurement data, the mean,

standard deviation, median, minimum, and maximum values were analyzed according to their distribution. In addition, the number of cases and percentages of each category were evaluated for classification indicators. The comparison of the basic data of the two groups was based on their distribution, using the student's t test or Wilcoxon rank sum test. Categorical variables were calculated using chi-square test or Fisher's exact probability method. The drawing of survival curve and the estimation of survival rate were performed using the Kaplan–Meier method, the overall comparison of the survival curve between groups was conducted using the log rank test, and the Cox proportional hazard model was used for the multivariate analysis and relative risk and its 95% CI estimate. All statistical analyses were performed according to the predetermined statistical analysis plan, and the statistical analysis report of the research results was written. However, it should be clarified that the actual sample size of this study did not reach the preset level, making it impossible to validate the research hypothesis; thus, only preliminary descriptions and explorations can be made.

Table 1 Baseline clinicopathologic characteristics

Characteristic	Group A ($n=11$)	Group B($n=11$)
Age at diagnosis, year	57(35–64)	55(37–67)
Tumor size		
≤ 2 cm	1(9.1%)	3(27.3%)
>2 cm	10(90.9%)	8(72.7%)
Tumor type & grade		
IDC II	7(63.6%)	2(18.2%)
IDC III	3(27.3%)	7(63.6%)
ILC	1(9.1%)	2(18.2%)
Ki-67		
≤ 25%	2(18.2%)	1(9.1%)
>25%	9(81.8%)	10(90.9%)
Scheme of NAC		
Standard-interval	3(27.3%)	3(27.3%)
Dose-dense	8(72.7%)	8(72.7%)
Type of surgery		
BCT + ALND	7(63.6%)	3(27.3%)
MRM	4(36.4%)	8(72.7%)
ypT0/is		
Yes	0(0)	2(18.2%)
No	11(100%)	9(81.8%)
Miller-Payne		
G1/2	3(27.3%)	2(18.2%)
G3/4/5	8(72.7%)	9(81.8%)

Group A: adjuvant intensive treatment group, *Group B*: control group, IDC: invasive ductal carcinoma, ILC: invasive lobular carcinoma, *NAC*: neoadjuvant chemotherapy, *BCT*: breast-conserving surgery, *ALND*: axillary lymph node dissection, *MRM*: modified radical mastectomy, *ypT0/is*: no residual invasive tumor cells in the breast

Results

Due to the slow progress of enrollment, at its regular meeting on March 29, 2022 the Data and Safety Monitoring Committee recommended stopping the trial as it was unlikely completed on time, despite the enrollment rate exceeding 60%. Data cutoff for this report was April 4, 2022. Twenty-two eligible patients were enrolled between November 2017 and March 2022. Among them, 11 patients were randomly allocated to the vinorelbine intensive treatment group (group A), whereas the other 11 patients were allocated to the control group (group B). The baseline characteristics of the two groups of patients are shown in Table 1, and the median age of the enrolled patients was 55 years (35–67 years). Approximately 81.8% of the patients had a clinical tumor stage T2 or higher. The NAC regimen for all patients was four cycles of anthracycline followed by four cycles of paclitaxel; 72.7% of the enrolled patients used a dose-dense anthracycline regimen (epirubicin 100 mg/m^2+cyclophosphamide 600 mg/m^2, d1, q2w) and 27.3% used the conventional 3-week anthracycline regimen (epirubicin 100 mg/m^2+cyclophosphamide 600 mg/m^2, d1, q3w). Paclitaxel was administered as a single-week regimen (80 mg/m^2, d1, d8, d15, qw).

Clinical trial observation, patient follow-up, and data summarization were completed early in January 2023. The last follow-up date was April 12, 2023, and the median follow-up duration was 36 months (1–65 months). In the observation group, one patient showed no abnormalities in the preoperative baseline examination; however, the patient developed a sudden onset of abdominal distension and abdominal pain while preparing for radiation therapy 1 month after the surgery. Abdominal computed tomography re-examination revealed multiple hepatic masses, and metastasis was considered. The patient died of hepatic encephalopathy 1 month after randomization. Regarding the primary endpoint, the 3-year DDFS rate in the vinorelbine intensive treatment group was significantly higher than that in the control group (90.0% vs. 42.4%, log-rank $P=0.022$) (Fig. 2A). Regarding the secondary endpoints, the 3-year RFS rate was significantly higher in the vinorelbine intensive treatment group than in the control group (90.0% vs. 42.4%, log-rank $P=0.022$) (Fig. 2B). No significant difference was observed in the 3-year OS rate between the two groups, but there was a trend of benefit in the intensive treatment group (90.0% vs. 61.4%, log-rank $P=0.149$) (Fig. 2C).

Multivariate analysis showed that the control group had more survival events than the intensive treatment group. The difference in DDFS (HR=0.19; 95% CI, 0.02–1.76), RFS (HR=0.19; 95% CI, 0.02–1.76), and OS (HR=0.32; 95% CI, 0.03–3.42) between the two groups showed a trend but without statistical significance (Table 2).

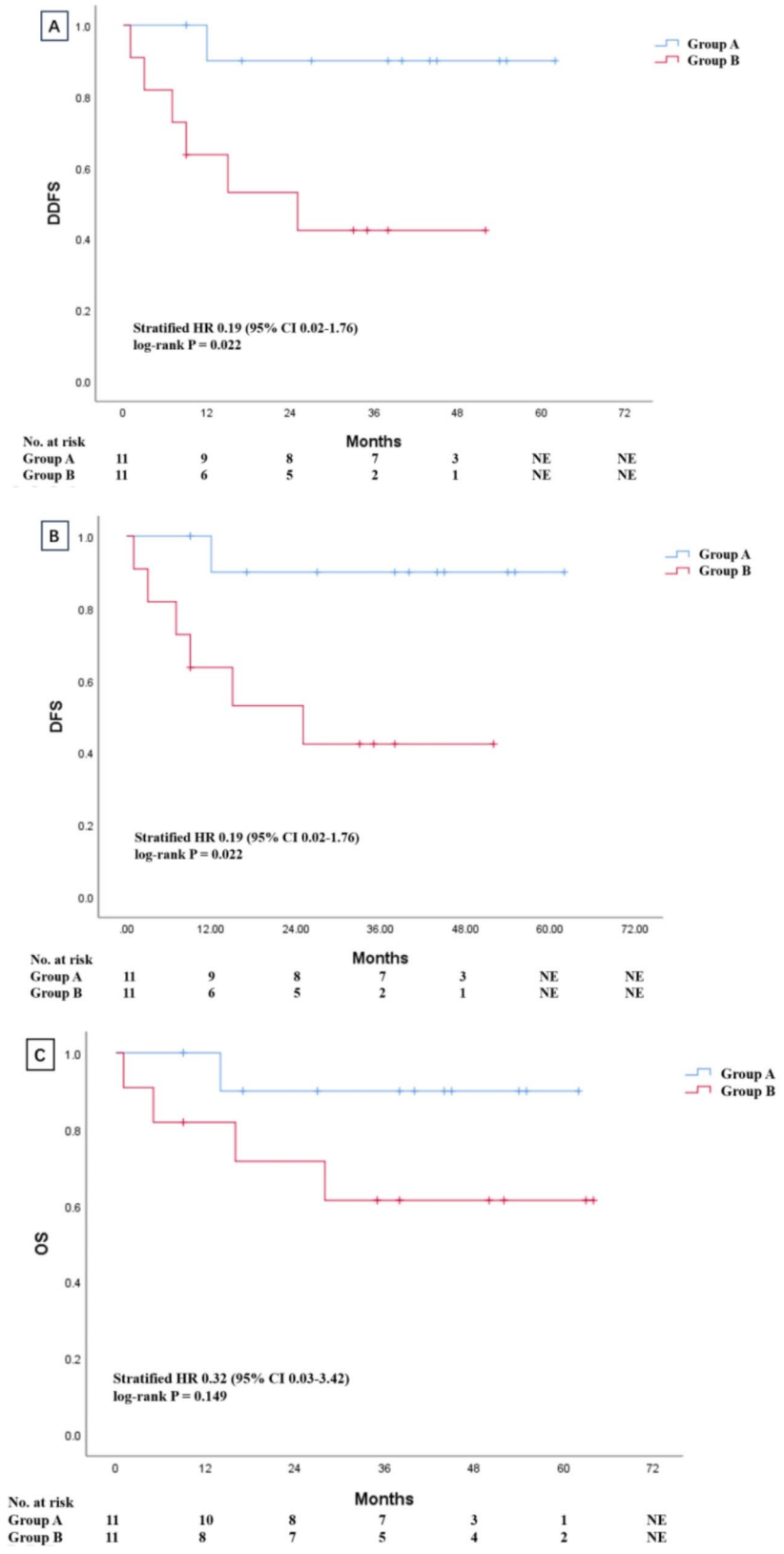

Fig. 2 Kaplan-Meier estimates for Distant Disease-Free Survival **(A)** and Recurrence-Free Survival **(B)** and Overall Survival **(C)** according to treatment group. Group A: adjuvant intensive treatment group; Group B: control group

Table 2 Multivariate analyses for the effect of random group and type of surgery on survival

Characteristic	DDFS		RFS		OS	
	HR(95%CI)	*P*-value*	HR(95%CI)	*P*-value*	HR(95%CI)	*P*-value*
Type of group		0.145		0.145		0.350
Group A	0.19(0.02–1.76)		0.19(0.02–1.76)		0.32(0.03–3.42)	
Group B	1		1		1	
Type of surgery		0.260		0.260		0.482
BCT + ALND	0.28(0.03–2.56)		0.28(0.03–2.56)		0.43(0.04–4.55)	
MRM	1		1		1	

HR: hazard ratio, *DDFS*: distant disease-free survival, *RFS*: recurrence-free survival, *OS*: overall survival

Group A: adjuvant intensive treatment group, *Group B*: control group, *BCT*: breast-conserving surgery, *ALND*: axillary lymph node dissection, *MRM*: modified radical mastectomy

**P*-value < 0.05 is statistically significant

Table 3 Adverse events assessed within 4 months after randomization

Event	Group A (*n* = 11)		Group B (*n* = 11)	
	Grade 1 or 2	Grade 3 or 4	Grade 1 or 2	Grade 3 or 4
Hematologic adverse event				
Neutropenia	6	1	0	0
Thrombocytopenia	1	0	0	0
Anemia	3	0	0	0
Febrile neutropenia (FN)	0	1	0	0
Nonhematologic adverse event				
Nausea	3	0	0	0
Vomiting	1	0	0	0
Diarrhea	0	0	0	0
Fatigue	4	0	0	0
Thrombophlebitis	0	0	0	0
Peripheral neurotoxicity	1	0	0	0
Aminotransferase increased	2	0	0	0
Hair loss	0	0	0	0

All patients completed vinorelbine adjuvant intensive chemotherapy with sufficient doses, and one patient (9%) manifested with grade 3 neutropenic fever, and treatment completion was delayed for 1 week. Due to the indwelling central venous catheter inserted in advance, no patient developed thrombophlebitis or other severe infusion adverse reactions. None of the patients had peripheral neurotoxicity above grade 3 or gastrointestinal symptoms, such as nausea, vomiting, and diarrhea. The interval between the start of intensive treatment and the last NAC was less than 2 months, and no adverse reactions of hair loss were observed (Table 3).

Discussion

To the best of our knowledge, this is the first randomized controlled study on vinorelbine as an adjuvant intensive therapy for TNBC patients with lymph node non-pCR after standard NAC. Although the enrollment was not completed as planned, the 3-year DDFS rate and RFS rate in the intensive treatment group were significantly higher than those in the control group (90.0% vs. 42.4%, $P=0.022$, both), and the OS rate showed a trend of benefit in the intensive treatment group (90.0% vs. 61.4%, $P=0.149$). It is possible to obtain more meaningful research results if more patients are enrolled and the follow-up time is prolonged.

The study extended beyond the planned duration of 3 years, lasting for a period of 4 years and 5 months from the enrollment of the first patient in November 2017 to the enrollment of the last patient in March 2022. A total of 22 patients were enrolled, accounting for only 7.2% (22/304) of the study's predetermined sample size. The inclusion criteria for this study were limited to patients who achieved positive lymph node pCR, based on previous research [7].

The reasons why the actual enrollment of patients was significantly less than planned are as follows: (1) The proportion of TNBC was less (9%) than that reported in previous studies (12–17%) [3], possibly due to the negative standard of immunohistochemical HR/HER-2 detection (e.g.HR < 10% change to HR < 1%). The inclusion criteria for this study were limited to patients with initial positive axillary lymph node puncture, resulting in a higher pCR rate in the axillary lymph nodes compared to the breast tumor. Undoubtedly, this increased the complexity of patient selection. (2) Since 2017, our center has gradually adjusted the neoadjuvant therapy for patients with TNBC and HER-2-positive breast cancer from the conventional 3-week anthracycline followed by a single-week paclitaxel regimen to an intensive 2-week anthracycline followed by a single-week paclitaxel regimen, which has increased the absolute value of the pCR rate of breast cancer primary tumor and lymph node by 11% and 14.2%, respectively [13]. (3) During the later stage of enrollment, the coronavirus disease 2019 pandemic occurred, and the number of new breast cancer patients diagnosed and treated at our center declined by 60% compared with the same period in previous years. Due to the changes in the hospital management model and the frequency of patient visits, it was more difficult to

enroll patients in clinical research. (4) The results of the CREATE-X study were published in June 2017 [8]. Since then, six to eight cycles of intensive capecitabine therapy after surgery has become the recommendation of major guidelines for TNBC that failed to achieve pCR with NAC. However, the enrollment population of this study overlapped with the application population of the CREATE-X study, which undoubtedly increased the difficulty of enrollment.

The CREATE-X study enrolled 601 hormone-receptor-positive patients (67.8%) and 347 patients (39.1%) with negative axillary lymph nodes (including baseline negative and lymph node pCR). In the subgroup analysis, these two groups of patients did not obtain a DFS benefit from intensive capecitabine therapy (HR, 0.81; 95CI%, 0.55–1.17. HR, 0.87; 95CI%, 0.48–1.60). Furthermore, the primary endpoint of this study was DDFS rather than DFS in the CREATE-X study. The distant metastasis could be used as a criterion for determining the efficacy of intensive adjuvant chemotherapy, and DFS or RFS would be affected by local treatment factors, such as local recurrence and second primary cancer. These factors all indicated that the population and observation endpoints of this study were more specific.

Oral vinorelbine formulations are more acceptable to patients than IV administration and have more advantages in clinical management and adverse reactions [10, 14, 15]. A real-world study has shown that oral vinorelbine monotherapy or combination therapy had good efficacy and tolerability compared with IV administration in patients with previously treated advanced breast cancer [16]. However, at the beginning of this study, evidence that the oral vinorelbine was as effective as the standard IV vinorelbine regimen for breast cancer was not found; thus, the intensive treatment group in this study used IV rather than oral vinorelbine.

Similar to capecitabine, vinorelbine could not replace anthracycline and paclitaxel in chemotherapy regimens for early breast cancer; however, it could be used as their supplement. Minckwitz et al. [17] showed that in the neoadjuvant treatment stage, in patients who did not achieve early remission with TAC×2, switching to vinorelbine+capecitabine (NX) regimen for four cycles, compared with continuing TAC×4, could prolong DFS (HR, 0.59; 95% CI, 0.49 to 0.82; $P<0.001$). Shannon et al. [18] used vinorelbine combined with Herceptin as adjuvant therapy in 30 patients with early HER-2 positive breast cancer who did not receive the standard TH regimen for various reasons. With a median follow-up of 68 months, the 5-year IDFS rate was 90.9%, including one case of local recurrence and one case of distant metastasis. The 5-year OS rate was 100%. Thus far, few reports on the application of vinorelbine in the neoadjuvant and adjuvant treatment of early TNBC exist.

The limitations of this study include the extremely limited number of recruits, resulting in an inadequate sample size. Furthermore, there was an imbalance between the groups. These factors may have a detrimental impact on the reliability and generalizability of the study results, thereby constraining the validity of the study conclusions.

In conclusion, although adjuvant intensive vinorelbine therapy demonstrates clinical effectiveness and good tolerability for TNBC patients with residual cancer in the lymph nodes, it is important to note that due to the limited sample size, definitive conclusions cannot be drawn. Therefore, further randomized studies with larger sample sizes are necessary to validate this finding.

Acknowledgements
This work was supported by the Clinical Research Fund For Distinguished Young Scholars of Peking University Cancer Hospital(Code:QNJJ2023010) and the Horizontal topic(Code:2-3-1-16-077).

Author contributions
X.W., Y.H., Z.F., and T.O. contributed to the conceptualization, formal analysis, and writing-original draft. X.W. collected, analyzed and interpreted the data, and was a major contributor in writing the manuscript. All authors contributed to data curation, investigation, methodology, project administration, and writing, review and editing. All authors read and approved the final manuscript.

Funding
This work was funded by Jiangsu Haosen Pharmaceutical Group Co., Ltd., and vinorelbine for injection (Gaynor) test drug and subclavian puncture catheter materials were provided free of charge. The sponsors were not involved in any matters related to the trial design, data collection and analysis, or interpretation of results.

Data availability
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Peking University Cancer Hospital prior to initiation. Ethical approval date was August 21, 2017.

Consent to participate
Informed consent was obtained from all individual participants included in the study.

Consent to publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 21 August 2024 / Accepted: 4 November 2024
Published online: 27 November 2024

References
1. Zheng R, Zhang S, Zeng H, et al. Cancer incidence and mortality in China, 2016. J Natl Cancer Cent. 2022;2(1):1–9.
2. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17–48.

3. Foulkes WD, Smith IE, Reis-Filho JS. Triple-negative breast cancer. N Engl J Med. 2010;363(20):1938–48.
4. Dent R, Trudeau M, Pritchard KI, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res. 2007;13(15 Pt 1):4429–34.
5. von Minckwitz G, Untch M, Blohmer JU, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. J Clin Oncol. 2012;30(15):1796–804.
6. Wang X, He YJ, Ying M, et al. Impact of response of positive axillary nodes to neoadjuvant chemotherapy on breast cancer survival. Zhonghua Yi Xue Za Zhi. 2011;91(30):2116–9.
7. Wang X, He YJ, Li JF, et al. Impact of adjuvant chemotherapy on the prognosis of hormone receptor negative breast cancer with residual lymph node disease after neoadjuvant chemotherapy. Zhonghua Yi Xue Za Zhi. 2017;97(20):1576–9.
8. Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast Cancer after preoperative chemotherapy. N Engl J Med. 2017;376(22):2147–59.
9. Fumoleau P, Delgado FM, Delozier T, et al. Phase II trial of weekly intravenous vinorelbine in first-line advanced breast cancer chemotherapy. J Clin Oncol. 1993;11(7):1245–52.
10. Freyer G, Delozier T, Lichinister M, et al. Phase II study of oral vinorelbine in first-line advanced breast cancer chemotherapy. J Clin Oncol. 2003;21(1):35–40.
11. Chua S, Smith IE, A'Hern RP, et al. Neoadjuvant vinorelbine/epirubicin (VE) versus standard adriamycin/cyclophosphamide (AC) in operable breast cancer: analysis of response and tolerability in a randomised phase III trial (TOPIC 2). Ann Oncol. 2005;16(9):1435–41.
12. Ogston KN, Miller ID, Payne S, et al. A new histological grading system to assess response of breast cancers to primary chemotherapy: prognostic significance and survival. Breast. 2003;12(5):320–7.
13. Wang X, Wang J, He Y, et al. Observation Effectiveness of dose-dense neoadjuvant Anthracycline Sequential Weekly Paclitaxel for Triple-negative breast Cancer patients. Clin Breast Cancer. 2023;23(4):423–30.
14. Aapro M, Finek J. Oral vinorelbine in metastatic breast cancer: a review of current clinical trial results. Cancer Treat Rev. 2012;38(2):120–6.
15. Steger GG, Dominguez A, Dobrovolskaya N, et al. Single-Agent oral vinorelbine as first-line chemotherapy for endocrine-pretreated breast Cancer with bone metastases and no visceral involvement: NORBREAST-228 phase II study. Clin Breast Cancer. 2018;18(1):e41–7.
16. Heudel P, Delaloge S, Parent D, et al. Real-world evaluation of oral vinorelbine in the treatment of metastatic breast Cancer: an ESME-MBC Study. Anticancer Res. 2020;40(7):3905–13.
17. von Minckwitz G, Blohmer JU, Costa SD, et al. Response-guided neoadjuvant chemotherapy for breast cancer. J Clin Oncol. 2013;31(29):3623–30.
18. McLaughlin S, Nakajima E, Bar Y, et al. Adjuvant trastuzumab and vinorelbine for early-stage HER2 + breast cancer. Ther Adv Med Oncol. 2023;15:17588359221146133.

Publisher's note