Clinicopathologic analysis of 722 breast cancer patients who met the inclusion criteria of the TAILORx trial

Hong-Yu Xiang¹, Yin-Hua Liu¹, Hong Zhang², Shuang Zhang², Ling Xin¹, Ling Xu¹, Jing-Ming Ye¹, Ting Li², Xue-Ning Duan¹, Qian Liu¹

¹Breast Disease Center, Peking University First Hospital, Beijing 100034, China; ²Department of Pathology, Peking University First Hospital, Beijing 100034, China.

Abstract

Background: The results of the Trial Assigning IndividuaLized Options for Treatment (TAILORx) suggested that approximately 70% of T1-2N0M0, hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer patients can avoid chemotherapy and receive only adjuvant endocrine therapy. We conducted a retrospective analysis of the clinicopathologic features and prognostic factors of patients with breast cancer who met the inclusion criteria of the TAILORx trial.

Methods: According to the enrollment criteria of the TAILORx trial, a retrospective analysis was performed on patients with breast cancer who were treated from January 2008 to December 2015 at Peking University First Hospital. The clinicopathologic characteristics of all patients were analyzed, and prognoses were calculated using the Kaplan-Meier method and a Cox proportional hazards model.

Results: A total of 2430 patients with early stage breast cancer who were admitted to our hospital had complete clinicopathologic data and follow-up information. Of these patients, 722 met the inclusion criteria and were enrolled in the present study, accounting for 29.7% of all patients. Among them, 417 (57.8%) patients received only adjuvant endocrine therapy (the non-chemo group), and 305 (42.2%) patients received adjuvant chemotherapy followed by adjuvant endocrine therapy (the chemo group). No statistically significant difference was observed in overall survival (OS) between the two groups (non-chemo vs. chemo: 5-year OS: 97.9% vs. 97.9%, χ² = 1.00, P = 0.995; hazard ratio [HR] = 1.00, 95% confidence interval [CI]: 0.46–2.21). A significant difference was observed in disease-free survival (DFS) between the two groups (non-chemo vs. chemo: 5-year DFS: 97.9% vs. 94.7%, χ² = 8.65, P = 0.003; HR = 3.05, 95% CI: 1.40–6.67). The choice of adjuvant therapy was associated with clinicopathologic factors, such as the age at diagnosis, T stage, histologic grade, the Ki67 index, the presence of intravascular tumor thrombus (P < 0.001), pathologic type, and menstrual status (P = 0.014).

Conclusions: In the absence of internationally recognized multigene testing methods, for patients with early hormone receptor-positive, HER2-negative breast cancer, clinicians can develop a treatment plan based on clinicopathologic features only, which can effectively screen some patients who do not need adjuvant chemotherapy. However, nearly half of patients still receive adjuvant chemotherapy, and whether these patients can be exempted from chemotherapy warrants further exploration.

Keywords: Adjuvant therapy; Early stage breast cancer; Multigene detection; Prognosis; TAILORx trial

Introduction

Whether patients with early stage breast cancer should receive adjuvant chemotherapy is controversial. Multigene panel assays have been used widely as genomic predictors of the chemotherapy response and prognosis of patients with breast cancer in the western world. The Trial Assigning IndividuaLized Options for Treatment (TAILORx) enrolled patients with T1-2N0M0, hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer and detected them all with the Oncotype Dx 21-gene Breast Cancer Recurrence Score (RS)® (Genomic Health, Redwood City, CA, USA) assay. The results suggested that patients with an RS score of 0 to 25 could be exempted from chemotherapy and receive only adjuvant endocrine therapy. However, multigene panel assays were not certified and accessible in China until September 2018. To study the patients who met the enrollment criteria of the TAILORx trial in China and understand the reference basis on which clinicians made different treatment decisions for this population in the absence of multigene detection, we conducted a single-center retrospective analysis of patients with early stage breast cancer who met the inclusion criteria of the TAILORx trial.
invasive breast cancer who were admitted and treated from January 1, 2008 to December 31, 2015, at Peking University First Hospital.

Methods

Ethical approval

Ethical approval from the Institutional Ethics Examining Committee of Human Research of Peking University First Hospital (No. 2019-14) was obtained prior to patient recruitment. All participants signed a written informed consent form after a full explanation of the study was provided, including the schematic procedures and potential benefits and complications.

Participants

The present study was a retrospective descriptive review of data from patients with early stage invasive breast cancer who were treated at Peking University First Hospital from January 1, 2008, to December 31, 2015. Clinical staging of all patients was performed referring to the American Joint Committee on Cancer (AJCC) tumor node metastasis staging system for breast cancer (8th edition) while molecular subtyping was confirmed based on the 2011 St. Gallen consensus criteria. All histopathologic evaluations were reperformed by experienced pathologists from the hospital’s Pathology Department based on the latest guidelines.

Study design

The inclusion criteria for the study were determined with reference to the TAILORx trial and included the following: (a) aged 18 to 75 years; (b) a tumor diameter of 1.1 to 5.0 cm (or 0.6–1.0 cm and a histologic grade of 3) (T1b-2); (c) negative axillary lymph nodes (N0); (d) no distant metastasis (M0); (e) hormone receptor (estrogen receptor [ER] and/or progesterone receptor [PR]) positivity; (f) HER2 negativity; (g) no preoperative treatment; (h) received surgical treatment; and (i) received standard endocrine therapy. Among them, patients who received endocrine therapy alone were identified as the non-chemo group, and patients who received adjuvant chemotherapy followed by endocrine therapy were identified as the chemo group.

Histopathologic immunohistochemistry, histologic grades, and interpretation criteria

To detect ER and PR positivity, an ER antibody (clone: 1D5, dilution: 1:200; Dako, Glostrup, Denmark) and a PR antibody (clone: 16 + SAN27, dilution: 1:200, Novocastra, DE) were used. Staining was performed using an automatic immunohistochemical staining machine (Autostainer Link 48; Dako). The ER and PR antibodies were incubated with the sections at 37°C for 20 min. Staining was performed according to the 2010 guidelines of the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) for immunohistochemical detection of ER/PR in breast cancer. ER/PR positivity was defined as ≥1% tumor cell nuclear staining, and ER/PR negativity was defined as <1% tumor cell nuclear staining in the presence of positive internal control.

For HER2 detection, a HER2 antibody (clone: rabbit monoclonal antibody 4B5; Ventana, Tucson, AZ, USA) was used. Staining was performed using an automatic immunohistochemical staining machine (Benchmark XT, Ventana, Tucson, AZ, USA). The HER2 antibody was incubated with the sections at 37°C for 16 min. According to the 2013 ASCO/CAP guidelines for HER2 detection, the criteria for HER2 positivity were as follows: (by immunohistochemistry) greater than 10% of cells within the field of view with complete and intense circumferential membrane staining (by fluorescence in situ hybridization [FISH]) an average HER2 copy number ≥6.0 signals/cell, or (by FISH) a Dual-probe HER2/chromosome 17 centromere (CEP17) ratio ≥2.0 when 20 or more cells in the region were counted and detected.

A Ki67 antibody (clone: MIB1, dilution: 1:200; Dako) was used, and staining was performed using an automated immunohistochemical staining machine (Autostainer Link 48; Dako). The percentage of positive cells among 1000 invasive carcinoma tumor cells was determined. According to the 2018 Chinese Society of Clinical Oncology (CSCO) breast cancer guidelines, a Ki67 index <15% was defined as low expression, while a Ki67 index >30% was defined as high expression. The Nottingham Combined Histologic Grade Scale was used. The following histologic grading indicators of invasive breast cancer were used: gland tubule formation, nuclear size and shape, chromatin atypia, and mitotic figures, which were divided into grades 1, 2, and 3.

Risk categories

The 10th St. Gallen consensus of risk categories defined for patients with breast cancer was used. All patients were divided into low-risk, intermediate-risk, and high-risk categories. Low risk was defined as negative lymph node involvement with all the following characteristics: pathologic tumor diameter (pT) ≤2 cm, histologic grade = 1, the absence of extensive vascular tumor thrombus, ER and/or PR positivity, HER2 negativity, and age ≥35 years. The intermediate risk was defined as negative lymph node involvement and at least one of the following characteristics: pT >2 cm, histologic grade = 2 to 3, extensive vascular tumor thrombus, ER and PR negativity, HER2 overexpression, or age <35 years. High risk was defined as ≥4 lymph node metastases or as 1 to 3 lymph node metastases with ER and/or PR negativity or HER2 positivity.

Follow-up

All patients underwent physical, laboratory, and imaging examinations based on the Chinese Guidelines for the Diagnosis and Treatment of Breast Cancer (2018). All follow-up data were obtained from outpatient medical records as well as telephone and mail inquiries and were updated until June 30, 2019. The follow-up data include disease-free survival (DFS) and overall survival (OS). DFS
was defined as the time from the diagnosis of the disease to the diagnosis of local or contralateral breast cancer recurrence or distant metastasis. OS was defined as the time from the diagnosis of the disease to death from any cause.

**Statistical analysis**

Descriptive statistics were used to describe patient characteristics. Groups were compared by Student’s t test for continuous data, the Pearson Chi-squared test for categorical variables and the Mann-Whitney U test for grading variables. Survival analyses were calculated using the Kaplan-Meier method and a Cox proportionate hazards model. The intergroup comparison of DFS and OS was performed using the log-rank test. The test standard for all statistical methods was set to the 0.05 level. All tests were two-sided analyses. Analyses were conducted using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA).

**Results**

**General information**

From January 1, 2008, to December 31, 2015, 2430 patients with early stage invasive breast cancer with complete clinicopathologic information and follow-up data were treated at our hospital; the median age of these patients was 54 years (range, 21–75 years). Among them, 722 patients met the inclusion criteria and were enrolled in the present study, accounting for 29.7% of all patients with early stage breast cancer. Among all enrolled patients, PR status, and the presence of nerve invasion were similar between the two groups [Table 1].

**Prognostic analysis**

All enrolled patients were followed for a median time of 73 months. The 5-year OS rate was 97.9%, and the 5-year DFS rate was 96.5%. Both 5-year OS rates in the chemo group and the non-chemo group were 97.9% (P = 0.995). The 5-year DFS rates in the chemo group and the non-chemo group were 94.7% and 97.9%, respectively. A significant difference was observed in DFS between the two groups (P = 0.003). Although the Cox regression analysis showed no significant difference in OS (hazard ratio [HR]: 1.00, 95% confidence interval [CI]: 0.46–2.21), a higher probability of recurrence and metastasis was observed in the chemo group (HR: 3.05, 95% CI: 1.40–6.67) [Figure 1 and Table 2].

**Clinical risk evaluation and treatment regimen selection**

According to the 10th St. Gallen consensus of risk category definitions for breast cancer patients, 223 (30.9%) patients were evaluated as low risk, 499 (69.1%) patients were evaluated as intermediate risk, and no one was categorized as high risk. Among the low-risk patients, 181 (81.2%) patients received only adjuvant endocrine therapy, while the remaining 42 (18.8%) patients received adjuvant chemotherapy followed by endocrine therapy. Among the intermediate-risk patients, 263 (52.7%) patients received adjuvant chemotherapy, and 236 (47.3%) patients received adjuvant endocrine therapy alone. Patients with intermediate risk in the chemo group were significantly more than those in the non-chemo group (P < 0.001). Among the intermediate-risk patients, DFS in the non-chemo group was significantly higher than that in the chemo group (P = 0.007), but no significant difference was found in OS between the two groups (P = 0.746). The Cox regression analysis showed the same results as the Kaplan-Meier analyses (DFS: HR: 3.57, 95% CI: 1.34–9.48; OS: HR: 0.87, 95% CI: 0.38–2.01) [Table 3].

**Discussion**

The TAILORx trial is a large multicenter phase III clinical randomized controlled trial supported by the National Cancer Institute of the United States targeting early stage invasive breast cancer. The trial aimed to investigate whether patients with different RSs on the Oncotype DX® assay can be exempted from chemotherapy. The results of the trial were first published in 2015 and suggested that patients with an RS of 0 to 10 can be exempted from chemotherapy and receive only adjuvant endocrine therapy. The subsequent results showed that patients with an RS of 11 to 25 can also be exempted from chemotherapy. At the 2019 ASCO meeting, the researchers presented the latest results of the TAILORx trial, which revealed that clinical risk stratification provided additional prognostic information to identify premenopausal women who could benefit from more effective therapy.
In 2018, the 8th edition of the AJCC staging manual noted the importance of five multigene tests, including Oncotype DX® and MammaPrint®, in the clinical diagnosis and treatment of breast cancer with high-level evidence.[4] In 2018, the National Comprehensive Cancer Network clinical practice guidelines for breast cancer also stated that T1-2N0M0, ER-positive, and HER2-negative breast cancers were indications for Oncotype DX® detection with Class I evidence.[14] The Oncotype DX®[15] and MammaPrint®[16] tests have been recommended and certified by many international consensuses and guidelines. According to a multicenter study performed in the United States, from 2011 to 2014, more than 30% of patients with breast cancer received multigene testing, and the Oncotype DX® test was used in more than 90% of the cases. Multigene signature panel (MSP) use has increased over time and is associated with a decreased rate of chemotherapy administration (24.6% MSP vs. 37.2% no MSP; P < 0.001).[17] However, in China, no internationally certified MSP was permitted into the market until MammaPrint® received approval in September 2018, which is why no patients underwent multigene testing in the present study. Our research aimed to demonstrate through real-world data how treatment decisions were made by clinicians without the support of MSP data and the clinical outcomes of HER2-negative, ER/PR-positive, early stage breast cancer patients.

In the present study, the cases that met the enrollment criteria accounted for 29.7% of all patients, suggesting

### Table 1: Baseline clinicopathologic characteristics in the chemo and non-chemo groups.

| Parameters                          | Chemo group (n = 417) | Non-chemo group (n = 305) | Statistics | P     |
|-------------------------------------|-----------------------|---------------------------|------------|-------|
| Age at diagnosis (years)            | 51.3 ± 10.5           | 56.5 ± 11.2               | −5.242*    | <0.001|
| Menopause                           |                       |                           | 5.981†     | 0.014 |
| Yes                                 | 242 (58.0)            | 149 (48.9)                |            |       |
| No                                  | 175 (42.0)            | 156 (51.1)                |            |       |
| T stage                             |                       |                           | 20.849†    | <0.001|
| T1                                  | 327 (78.4)            | 192 (6.0)                 |            |       |
| T2                                  | 90 (21.6)             | 113 (37.0)                |            |       |
| ER                                  |                       |                           |            |       |
| Positive                            | 412 (98.8)            | 295 (96.7)                | 3.745†     | 0.053 |
| Negative                            | 5 (1.2)               | 10 (3.3)                  |            |       |
| PR                                  |                       |                           | 0.475†     | 0.491 |
| Positive                            | 26 (6.2)              | 23 (7.5)                  |            |       |
| Negative                            | 391 (93.8)            | 282 (92.5)                |            |       |
| Pathologic type                     |                       |                           | 6.070†     | 0.014 |
| Non-special                         | 358 (85.9)            | 280 (91.8)                |            |       |
| Special                             | 59 (14.1)             | 25 (8.2)                  |            |       |
| Histologic grade                    |                       |                           | −10.190‡   | <0.001|
| Grade 1                             | 220 (52.8)            | 61 (20.0)                 |            |       |
| Grade 2                             | 175 (42.0)            | 167 (54.8)                |            |       |
| Grade 3                             | 22 (5.3)              | 77 (25.2)                 |            |       |
| Ki67 index                          |                       |                           | −9.674‡    | <0.001|
| <15%                                | 191 (45.8)            | 60 (19.7)                 |            |       |
| 15–30%                              | 185 (44.4)            | 127 (41.6)                |            |       |
| >30%                                | 41 (9.8)              | 118 (38.7)                |            |       |
| Vascular tumor thrombus             |                       |                           | 16.663‡    | <0.001|
| Yes                                 | 408 (97.8)            | 278 (91.1)                |            |       |
| No                                  | 9 (2.2)               | 27 (8.9)                  |            |       |
| Nerve invasion                      |                       |                           | 1.878†     | 0.171 |
| Yes                                 | 20 (4.8)              | 22 (7.3)                  |            |       |
| No                                  | 397 (95.2)            | 283 (92.7)                |            |       |

Values are presented as the mean ± standard deviation or n (%). *t values. †χ² values. ‡Z values. ER: Estrogen receptor; PR: Progesterone receptor.

### Table 2: Results of the Kaplan-Meier and Cox regression analyses in the chemo and non-chemo groups.

| Groups          | Overall survival | Disease-free survival |
|-----------------|------------------|-----------------------|
|                | n (%) | 5-year OS (%) | χ² | P      | HR (95%CI) | P      | n (%) | 5-year DFS (%) | χ² | P      | HR (95%CI) | P      |
| Chemo           | 11 (3.6) | 97.9 | 1.00 0.995 | 1.00 (0.46–2.21) | 0.995 | 21 (6.9) | 94.7 | 8.65 0.003 | 3.05 (1.40–6.67) | 0.005 |
| Non-chemo       | 14 (3.4) | 97.9 | 9 (2.2) | 97.9 |       |       |       |       |       |       |       |       |

OS: Overall survival; HR: Hazard ratio; CI: Confidence interval; DFS: Disease-free survival.
that the proportion of patients with early stage breast cancer who may be exempted from chemotherapy by multigene detection was less than 30%. Adjuvant chemotherapy remains an indispensable treatment method for more than 70% of patients with breast cancer, especially for breast cancer cases that are triple-negative, HER2-positive, and have ≥4 positive lymph nodes. A total of 57.8% of the patients received only adjuvant endocrine therapy, and the remaining 42.2% of patients received adjuvant chemotherapy followed by endocrine therapy. Significant differences in the age at diagnosis, menstrual status, T stage, pathologic type, histologic grade, the Ki67 index, and the presence of vascular tumor thrombus were observed between the two groups, which showed that these parameters were considered when clinicians made treatment decisions.

The 5-year DFS rate in the non-chemo group was higher than that in the chemo group (P = 0.003), suggesting that it was reliable for oncologists to screen patients with a low risk and exempt them from chemotherapy based on clinicopathologic characteristics. An age >40 years, postmenopausal status, T1 stage, a Ki67 index <15%, a special pathologic type, histologic grade 1, and the absence of vascular tumor thrombus constituted the main basis of such decisions. On the contrary, the 5-year OS rates in the two groups were similar (P = 0.995). We cannot determine whether all 42.2% of the patients truly benefited from chemotherapy according to existing data; perhaps this group of patients is more recommended to undergo multigene testing.

Since the beginning of the 21st century, treatment decision making based on the clinical risk category of breast cancer has received substantial attention. Since 2007, the St. Gallen consensus definitions and Adjuvant! Online have become widely accepted methods for risk classification in clinical practice and provide an important basis for selecting treatment regimens in clinical practice. In the present study, the enrolled patients were graded according to their risk categories based on the 10th St. Gallen consensus, and all patients met the criteria for clinically low- or intermediate-risk grading; none of the patients met the criteria for high-risk grading. Among all enrolled patients, 30.3% of the patients were evaluated as clinically low risk, and of these patients, 179 (81.7%) received only adjuvant endocrine therapy, suggesting that most low-risk patients avoided overtreatment according to clinical risk grading. The Microarray In Node negative Disease may Avoid ChemoTherapy (MINDACT) trial concluded that patients with a low clinical risk and a high risk of genetic testing failed to benefit from adjuvant chemotherapy. According to the conclusion of the MINDACT trial, 42 (18.8%) low-risk patients received unnecessary adjuvant chemotherapy in our study. Analysis of the clinicopathologic characteristics of these patients revealed
that a Ki67 index >15% and non-menopausal status were the main factors that influenced the oncologists in their selection of chemotherapy. A total of 70% of the patients were evaluated as clinically intermediate risk, 265 (52.7%) patients received only adjuvant endocrine therapy. DFS in the non-chemo group was significantly higher than that in the chemo group (P = 0.011), but no statistically significant difference in OS was found between the two groups (P = 0.746) in the intermediate-risk group. This result indicates that treatment decisions based on clinicopathologic characteristics alone for patients with an intermediate risk are lacking in clinical evaluations. Therefore, this population should become the indicated population for multigene detection.

This study has several limitations. First, this was a single-center study performed in a first-class hospital, and a selective bias was inevitable. Second, according to the policy in China, blood samples are not permitted to be sent abroad; thus, multigene detection was not undertaken in this cohort. Finally, the follow-up time was relatively short, and events were too rare to perform a stratified analysis, which caused the cross of the OS curve. Therefore, more detailed data with a longer follow-up time on a larger multicenter scale are encouraged to evaluate whether early stage breast cancer patients can be exempted from chemotherapy.

The level of standardized diagnosis and treatment of breast cancer has continuously improved, and multigene detection has established a new technology platform for clinical practice. The present study revealed that the proportion of patients with early stage breast cancer who have indications to receive multigene testing is less than 30%. Indications for multigene detection should be strictly controlled. At the same time, accurate and detailed clinicopathologic data are still the basis on which clinicians make treatment decisions. Patients with clinically low-risk breast cancer are not required to undergo multigene detection. However, utilizing multigene detection for clinically intermediate-risk patients can provide key information for making scientific treatment decisions.

**Funding**

This study was supported by a grant from the Beijing Medical Award Foundation (No. 2018-0304).

**Conflicts of interest**

None.

**References**

1. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Prospective validation of a 21-gene expression assay in breast cancer. N Engl J Med 2015;373:2005–2014. doi: 10.1056/NEJMoa150764.

2. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. N Engl J Med 2018;379:111–121. doi: 10.1056/NEJMoa1804710.

3. Sparano JA, Gray RJ, Ravdin PM, Makower DF, Pritchard KI, Albain KS, et al. Clinical and genomic risk to guide the use of adjuvant therapy for breast cancer. N Engl J Med 2019;380:2395–2405. doi: 10.1056/NEJMoa1904819.

4. Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, et al. American Joint Committee on Cancer (AJCC). AJCC cancer staging manual. 8th ed. New York: Springer; 2017.

5. Xu L, Li JH, Ye JM, Duan XN, Cheng YJ, Xin L, et al. A retrospective survival analysis of anatomic and prognostic stage group based on the American Joint Committee on Cancer 8th Edition Cancer Staging Manual in Lymph R Human Epidermal Growth Factor Receptor-2 negative Breast Cancer. Chin Med J 2017;130:1945–1952. doi: 10.4103/0366-6999.211896.

6. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thurlimann B, Senn HJ, et al. Strategies for subtypes—dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol 2011;22:1736–1747. doi: 10.1093/annonc/mdr304.

7. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol 2010;28:2784–2795. doi: 10.1200/JCO.2009.25.6529.

8. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, et al. Recommendations for the immunohistochemical testing of estrogen and progesterone receptors in breast cancer. N Engl J Med 2011;364:1827–1840. doi: 10.1056/NEJMoa1005890.

9. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thurlimann B, Senn HJ, et al. Assessment of Ki67 in breast cancer: recommendations from the International Ki67 in Breast Cancer working group. J Natl Cancer Inst 2011;103:1636–1644. doi: 10.1093/jnci/djr385.

10. Chinese Society of Clinical Oncology (CSCO) Breast Cancer Guideline (2018 v1) (in Chinese). Available from: http://www.gaca.org.cn/uploadfolder/files/201903/my27_998997.pdf. Accessed June 6, 2019.

11. Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. Histopathology 1991;19:403–410. doi: 10.1111/j.1365-2559.1991.tb00229.x.

12. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thurlimann B, Senn HJ, et al. Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer. Ann Oncol 2007;18:1133–1144. doi: 10.1093/annonc/mdm271.

13. National Health Commission of the People’s Republic of China. Chinese guidelines for diagnosis and treatment of breast cancer 2018 (English version). Chin J Cancer Res 2019;31:259–277. doi: 10.21147/jissn.1000-9604.2019.02.02.

14. Bevers TB, Helvie MA, Bonaccio E, Calhoun KE, Daly MB, Farrar WB, et al. Breast cancer screening and diagnosis, version 2018. NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2018;16:1362–1389. doi: 10.6004/jnccn.2018.0083.

15. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N Engl J Med 2004;350:2817–2826. doi: 10.1056/NEJMoa041588.

16. Van De Vijver MJ, He YD, Van’t Veer LJ, Dai H, Hart AA, Voskuil DW, et al. A gene-expression signature as a predictor of survival in breast cancer. N Engl J Med 2002;347:1999–2009. doi: 10.1056/NEJMoa021967.

17. Bhattacharyya N, Egger ME, Ajkay N, Scoggins CR, Martin RC, 2nd, McMasters KM. Multigene signature panels and breast cancer therapy: patterns of use and impact on clinical decision making. J Am Coll Surg 2018;226:406–412.e1. doi: 10.1016/j.jamcollsurg.2017.12.043.

18. Radivin PM, Sminoff LA, Davis GJ, Mercer MB, Hewlett J, Gerson N, et al. Computer program to assist in making decisions about adjuvant therapy for women with early breast cancer. J Clin Oncol 2001;19:980–991. doi: 10.1200/JCO.2001.19.4.980.

19. Cardoso F, van’t Veer LJ, Bogaerts J, Staets LS, Viale G, Delaforge S, et al. 70-Gene signature as an aid to treatment decisions in early-stage breast cancer. N Engl J Med 2016;375:717–729. doi: 10.1056/NEJMoa1602253.

How to cite this article: Xiang HY, Liu YH, Zhang H, Zhang S, Xin L, Xu L, Ye JM, Li T, Duan XN, Liu Q. Clinicopathologic analysis of 722 breast cancer patients who met the inclusion criteria of the TAILORS trial. Chin Med J 2019;132:2914–2919. doi: 10.1097/CM9.0000000000000548