Health-related quality of life of postmenopausal Chinese women with hormone receptor-positive early breast cancer during treatment with adjuvant aromatase inhibitors: a prospective, multicenter, non-interventional study

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Abstract

Background: Estimating quality of life (QoL) in patients with breast cancer is of importance in assessing treatment outcomes. Adjuvant endocrine therapy is widely used for hormone receptor-positive (HR+) early-stage breast cancer (EBC), and evidence suggests that aromatase inhibitors (AIs) may improve QoL for these patients. This study evaluated QoL in postmenopausal Chinese patients with HR+ EBC taking AIs.

Methods: This was a prospective, multicenter, and observational study that had no intent to intervene in the current treatment of recruited patients. Eligible patients were recruited within 7 days of beginning adjuvant treatment with AIs. The Functional Assessment of Cancer Therapy-Breast (FACT-B) scale was used to evaluate the patients’ QoL. Data were collected at baseline and at 6, 12, 18, and 24 months.

Results: From June 2010 to October 2013, a total of 494 patients with HR+ EBC were recruited from 21 centers. There was a 7.51-point increase in the patients’ mean FACT-B trial outcome index (TOI), from 90.69 at baseline to 98.72 at 24 months (P < .0001). The mean TOI scores at baseline, 6, 12, and 18 months were 90.69, 94.36, 97.71, and 96.75, respectively (P < .0001, for all). The mean (FACT-B) emotional well-being subscale scores at baseline, 6, 12, 18, and 24 months were 16.32, 16.55, 17.34 (P < .0001), 17.47 (P < .0001), and 17.85 (P < .0001), respectively, and social well-being scores were 18.61, 19.14 (P < .04), 19.35 (P < .008), 18.32, and 18.40, respectively. In the mixed model, baseline TOI, clinical visits, prior chemotherapies, age group, and axillary lymph-node dissection presented statistically significant effects on the change of FACT-B TOI and FACT-B SWB, whereas only baseline TOI, clinical visits, and prior chemotherapies presented statistically significant effects on the change of FACT-B EWB. FACT-B TOI, being the most pertinent and precise indicator of patient-reported QoL, demonstrated significant changes reflecting clinical benefit of adjuvant AIs endocrine therapy in the QoL of HR + EBC patients.

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Conclusions: The study demonstrated significant improvements in the long-term QoL of postmenopausal Chinese patients with HR+ EBC at 6, 12, 18, and 24 months after starting treatment with AIs. The current study indicates improved long-term QoL with AI adjuvant treatment, which will aid clinicians in optimizing treatment to yield effective healthcare outcomes.

Trial registration: Clinicaltrials.gov NCT01144572

Keywords: Quality of life, Prospective, Functional Assessment of Cancer Therapy-Breast, Trial outcome index, Hormone receptor-positive early-stage breast cancer postmenopause, Adjuvant, Aromatase inhibitors, Early breast cancer

Background
Breast cancer is the most common cancer in women worldwide, with nearly 1.7 million new cases diagnosed in 2012, representing about 12 % of all new cancer cases and 25 % of all cancers in women [1]. China accounts for nearly 12.2 % of all newly diagnosed breast cancer cases and about 9.6 % of all deaths from breast cancer worldwide [2]. In the past two decades, although the incidence of breast cancer has steadily increased, the death rate from the disease has declined [3]. Moreover, awareness of patients’ quality of life (QoL) during treatment is increasing, making it important for physicians and patients to consider therapeutic efficacy, safety of medical interventions, and QoL when selecting a treatment program. In addition, health-related QoL (HRQoL) is now being considered as an important end point in cancer clinical trials, which could contribute to improved treatment outcomes [4, 5].

Because various studies have consistently demonstrated superior efficacy and safety of the third-generation aromatase inhibitors (AIs) compared with those of tamoxifen alone in postmenopausal women with ER (+) breast cancer [6, 7], AIs are widely administered as standard adjuvant endocrine therapy in this population [8]. Previous researches suggested that treatment of patients with early-stage breast cancer (EBC) with third-generation AIs (e.g., anastrozole, letrozole, and exemestane) may improve their QoL [6–9]. However, this therapy is associated with persistent side effects and toxicity, which lead to negatively impact the patient’s QoL [10].

The Functional Assessment of Cancer Therapy-Breast (FACT-B), developed by Rush-Presbyterian-St. Luke’s Medical Center, Chicago, United States, is a widely used international scale to assess the QoL of patients with cancer [11, 12]. The use of such internationally consistent and validated scales to evaluate the QoL of Chinese patients will help improve the understanding of breast cancer outcomes. Specifically, they should enable physicians and patients to more clearly understand the long-term effects of AI therapy in breast cancer while making important treatment decisions. To date no nationwide, prospective, multicenter study has been available in China to evaluate the QoL of postmenopausal patients with early-stage breast cancer (EBC) positive (+) for hormone receptors (HR) treated with adjuvant therapy with AIs. It is of vital importance to evaluate the quality of life of Chinese patients using an internationally accepted method, so that the Chinese physicians are better knowledgeable about the effects of AIs on the long-term therapy when making therapeutic decisions. Because QoL studies can further indicate the directions needed for efficient treatment of cancer, the current study was conducted to evaluate the QoL of postmenopausal patients with HR (+) EBC receiving adjuvant treatment with AIs [13, 14].

Methods

Study design
This was the first prospective, multicenter, observational, non-interventional study in Chinese postmenopausal women [HR (+) and EBC] undergoing adjuvant treatment with AIs. There was no intent to intervene in the current treatment of the recruited patients (NCT01144572).

Participants
The following were the screening criteria: postmenopausal women, age ≤70 years, histologically documented HR (+) EBC, currently on adjuvant endocrine therapy with AIs and indications approved by the State Food and Drug Administration (SFDA), or AI adjuvant therapy started within the past 7 days. Women were eligible to be included in the study if they had simple mastectomy, breast-conserving surgery, or axillary lymph node dissection or sampling. Patients were excluded from the analysis if they were disinterested in participating, unable to adhere to the trial requirements for any reason, or were using AIs not approved by the SFDA for initial adjuvant endocrine therapy for EBC. Written informed consent for the data collection was obtained at the clinic visit after eligibility requirements were confirmed by the investigator. At any point during the study, patients could discontinue from the final analysis if it was their own decision, they had discontinued previous AI medication, or they had a documented evidence of disease relapse or progression.

The study was performed in accordance with Declaration of Helsinki and Good Clinical Practice Guidelines,
with approval obtained from each center’s independent ethics committee.

**Study objective**

The primary objective was to evaluate overall QoL in postmenopausal patients with HR(+) EBC during adjuvant treatment with AIs by assessing the change in the trial outcome index (TOI) of the FACT-B questionnaire from baseline to 24 months. The secondary objective was to evaluate the QoL in the same population during adjuvant treatment with AIs by examining FACT-B questionnaire results at several time points (baseline, 6, 12, and 18 months) on three FACT-B measures: TOI, emotional well-being (EWB) subscale scores, and social well-being (SWB) subscale scores. In addition, the factors affecting the QoL of patients with breast cancer were also determined.

**Data collection**

Data for demography and pathological examination for breast cancer were obtained for all the patients included in the analysis. Demographic parameters recorded were age, ethnic background, height, weight, basal metabolic index, and World Health Organization (WHO) performance status score. Pathological examination for breast cancer included assessment of the primary site, histological type, histological grading, and TNM stage. In addition, data were recorded for status of estrogen and progesterone receptors, history of breast cancer surgery, history of prior chemotherapy or radiotherapy, and use of AIs.

**Quality of life assessment**

QoL was assessed using the FACT-B questionnaire from baseline to 6, 12, 18, and 24 months. The TOI (sum of the physical well-being, functional well-being, and breast cancer–specific questions in the FACT-B) was regarded as the primary end point. An increase in TOI of more than 5 points from baseline, disease progression, or death was considered a clinically meaningful improvement in QoL. FACT-B instrument uses a 5-point rating scale, including measures for physical, social/family, emotional, and functional well-being. The instrument was used to inquire respondents on how true each statement was for the past 7 days and rate them. Response scales ranged from 0 (not at all) to 4 (very much). A one-on-one discussion was scheduled to collect data on demographic characteristics and QoL.

**Statistical methods**

The sample size was not formally calculated as this was a cohort study and there was no formal comparison between the groups. It was projected that 500 patients would
be enrolled within 3 years given the patient pool capacity in the participating sites. The primary QoL analysis, inclusive of all available questionnaires, was based on the patients who completed the informed consent form (ICF) and had one clinical visit included in the final analysis. The analysis was performed using the MIXED procedure of the SAS statistical software (SAS Institute, Cary, North Carolina, USA), which has the advantage of handling missing data without any imputation of missing values, provided that data are missing at random. Baseline covariates such as TOI score, prior chemotherapy (yes/no), age group, mastectomy (yes/no), and axillary clearance (yes/no) were included in the model regardless of statistical significance. This repeated measures analysis also included time from baseline, as both fixed and random polynomial effects, to allow patient-specific time trends and intercepts (described via random effects) to vary around an overall average trend and intercept (described via the fixed effects). The results of the analyses are presented in terms of adjusted means, associated confidence intervals (CIs), and P values. The mean score change from baseline was calculated for each patient with valid baseline questionnaires.

### Results

#### Patient disposition

From June 2010 to October 2013, a total of 494 patients were enrolled in the study; of these patients, 453 (91.7 %) completed the study and 41 (8.3 %) prematurely discontinued from the study as a result of loss to follow-up (5.1 %), disease relapse/progression (1.2 %), failure to adhere to inclusion/exclusion criteria (0.6 %), voluntarily discontinuation (0.4 %), cessation of AI therapy (0.4 %) and other (0.6 %). Thirty-one patients had at least one protocol violation, majorly because of failure to adhere

### Table 1 Baseline characteristics

| Parameter | N (missing) | Mean (SD) | Median | Min ~ max |
|-----------|-------------|-----------|--------|-----------|
| Weight (kg) | 486 (0) | 59.8 (8.93) | 59.0 | 35,105 |
| Height (cm) | 486 (0) | 159.4 (4.58) | 160.0 | 143,175 |
| BMI (kg/m²) | 486 (0) | 23.5 (3.25) | 23.0 | 16,39 |

#### WHO Performance Status Score

| Activities limited | 148 (30.5 %) |
|--------------------|--------------|
| Normal activities | 329 (67.7 %) |
| Bedridden time ≤ 50 % | 9 (1.9 %) |
| Total | 486 (100.0 %) |

#### Primary site

| Right breast | 240 (49.4 %) |
| Left breast | 243 (50.0 %) |
| Left breast, right breast | 3 (0.6 %) |
| Total | 486 (100.0 %) |

#### Histological type

| Invasive carcinoma | 463 (95.3 %) |
| Carcinoma in-situ | 23 (4.7 %) |
| Total | 486 (100.0 %) |

#### Histological grading

| Unevaluable(GX) | 58 (11.9 %) |
| Poorly differentiated(G3) | 84 (17.3 %) |
| Well differentiated(G1) | 56 (11.5 %) |
| Undifferentiated(G4) | 9 (1.9 %) |
| Moderately differentiated(G2) | 279 (57.4 %) |
| Total | 486 (100.0 %) |

#### ER status

| Positive | 471 (96.9 %) |
| Negative | 15 (3.1 %) |
| Total | 486 (100.0 %) |

#### PR status

| Positive | 387 (79.6 %) |
| Negative | 99 (20.4 %) |
| Total | 486 (100.0 %) |

#### ER and PR status

| ER positive,PR positive | 372 (76.5 %) |
| ER positive,PR negative | 99 (20.4 %) |
| ER negative,PR positive | 15 (3.1 %) |
| Total | 486 (100.0 %) |

#### Mastectomy

| No | 36 (7.4 %) |
| Yes | 450 (92.6 %) |
| Total | 486 (100.0 %) |

#### Breast-conserving surgery

| No | 450 (92.6 %) |

### Table 1 Baseline characteristics (Continued)

| Parameter | Yes | Total |
|-----------|-----|-------|
| Axillary lymph node dissection | 36 (7.4 %) | 486 (100.0 %) |
| Total | 486 (100.0 %) |
| Axillary lymph node sampling | 312 (64.2 %) | 486 (100.0 %) |
| Total | 486 (100.0 %) |
| Prior chemotherapy | 227 (46.7 %) | 486 (100.0 %) |
| Total | 486 (100.0 %) |
| Prior radiotherapy | 432 (88.9 %) | 486 (100.0 %) |
| Total | 486 (100.0 %) |
to inclusion criteria pertaining to postmenopausal women aged ≤70 years (n = 21), starting of AI adjuvant therapy within the past 7 days (n = 7), and unavailability of FACT-B data for clinical visits 2–5 (n = 8). Subsequently, a total of 486 patients (98.4 %) were included for the final analysis (Fig. 1).

Demographics and other baseline characteristics
All the 486 patients were of Chinese ethnic origin with a mean age of 57.3 years (range: 27–79 years), including 316 (65 %) women aged ≤60 years and 170 (35 %) women aged >60 years. Other baseline characteristics are listed in Table 1. Most patients had unilateral breast cancer, except three patients who reported bilateral primary breast cancer. More than half (372; 76.5 %) of the patients had estrogen receptor (ER, +)/progesterone receptor (PR, +) breast cancer, 99 (20.4 %) patients had ER(+)/PR(−) breast cancer, and 15 (3.1 %) patients had ER(−)/PR(+) breast cancer.

A total of 450 (92.6 %) patients had mastectomy, 36 (7.4 %) had breast-conserving surgery, 383 (78.8 %) had axillary lymph-node dissection, and 312 (64.2 %) had undergone axillary lymph-node sampling. Fifteen patients had an unknown AI use status; 426 patients were taking anastrozole, with 416 (97.7 %) treated for more than 2 years. The detailed information is given in Table 2. Among the 486 patients, only 1 patient reported hormone replacement therapy, 152 (31.3 %) patients were found to have major medical conditions other than breast cancer, and 92 (18.9 %) patients had major surgical therapies other than breast cancer surgery.

Primary endpoint-change in the FACT-B TOI from baseline to 24 months
A significant improvement was observed on the mean FACT-B TOI from baseline (mean: 90.69) to 24 months (mean: 98.72; P < .0001) (Table 3). In the MIXED model, baseline TOI, visit, prior chemotherapies, age group, and axillary lymph-node dissection presented statistically significant effects on the change of FACT-B TOI; however, mastectomy presented no statistically significant effects on the change of FACT-B TOI (Table 4). Lower boundary of the CI of the least squares (LS) mean (adjusted mean)

### Table 2 Use of aromatase inhibitors (final analysis set)

| Treatment duration (months) | Final analysis set (N = 486) n (%) |
|----------------------------|-----------------------------------|
| Anastrozole                |                                    |
| <6                         | 1 (0.2)                           |
| 6–12                       | 5 (1.2)                           |
| 12–18                      | 1 (0.2)                           |
| 18–24                      | 3 (0.7)                           |
| >24                        | 416 (97.7)                        |
| Total                      | 426 (100)                         |
| Missing                    | 15                                |
| Anastrozole/exemestane     |                                    |
| >24                        | 1 (100)                           |
| Total                      | 1 (100)                           |
| Anastrozole/letrozole      |                                    |
| >24                        | 5 (100)                           |
| Total                      | 5 (100)                           |
| Exemestane                 |                                    |
| >24                        | 10 (100)                          |
| Total                      | 10 (100)                          |
| Letrozole                  |                                    |
| 6–12                       | 2 (6.9)                           |
| >24                        | 27 (93.1)                         |
| Total                      | 29 (100)                          |

FACT-B: Functional Assessment of Cancer Therapy-Breast, SD standard deviation, TOI trial outcome index
change from baseline to 24 months in FACT-B TOI was >0, indicative of an increased TOI at 24 months of treatment. Moreover, LS mean change from 6 to 24 months of treatment was 4.48 (P < .0001). The LS mean of changes from baseline in FACT-B TOI with 95 % CIs is given in Table 4.

### Secondary end points

#### Changes in the FACT-B TOI from baseline to 6, 12, and 18 months

The mean FACT-B TOI was 90.69, 94.36, 97.71, and 96.75 at baseline, 6, 12, and 18 months, respectively, contributing to the increases from baseline 3.58, 7.03, and 5.18 at 6, 12, and 18 months, respectively (Table 3). The mean change in FACT-B TOI was significant at all time points as compared with baseline (P < .0001, for all).

#### Changes in the FACT-B EWB from baseline to 6, 12, 18, and 24 months

The mean FACT-B EWB was 16.32, 16.55, 17.34, 17.47, and 17.85 at baseline, 6, 12, 18, and 24 months, respectively, contributing to the mean increases from baseline 0.18, 1.03, 0.90, and 1.36 at 6, 12, 18, and 24 months, respectively (Table 5). The mean change in FACT-B EWB was significant at 12, 18, and 24 months as compared with baseline (P < .0001, for all).

In the MIXED model, baseline TOI, clinical visit, and prior chemotherapies had statistically significant effects on the change in FACT-B TOI, whereas age group, mastectomy, and axillary lymph-node dissection had no statistically significant effects on the change in FACT-B EWB (Table 6). In the MIXED model including baseline TOI, clinical visit, prior chemotherapies, age group, mastectomy, and axillary lymph-node dissection, the lower boundaries of the CIs of the LS mean (adjusted mean) changes from baseline to 12, 18, and 24 months in FACT-B EWB were all >0, indicating increased scores at 12, 18, and 24 months of treatment. The changes from 6 months of treatment to 12, 18, and 24 months of treatment are detailed in Table 6.

#### Changes in the FACT-B SWB from baseline to 6, 12, 18, and 24 months

The mean FACT-B SWB was 18.61, 19.14, 19.35, 18.32, and 18.40 at baseline, 6, 12, 18, and 24 months, respectively, contributing to the mean changes from baseline 0.18, 1.03, 0.90, and 1.36 at 6, 12, 18, and 24 months, respectively (Table 3). The mean change in FACT-B SWB was significant at 12, 18, and 24 months as compared with baseline (P < .0001, for all).

### Table 4 LS mean of changes from baseline in FACT-B TOI with 95 % CIs (final analysis set)

| Visit        | LS Mean | 95 % CI      | P value |
|--------------|---------|--------------|---------|
| 6 months     | 4.04    | 1.64–6.43    | –       |
| 12 months    | 7.10    | 4.57–9.63    | –       |
| 18 months    | 6.54    | 3.84–9.25    | –       |
| 24 months    | 8.51    | 5.75–11.27   | –       |
| 6–12 months  | −3.06   | −4.06 to –2.06 | <.0001 |
| 6–18 months  | −2.50   | −3.83 to –1.17 | .0002  |
| 6–24 months  | −4.48   | −5.96 to –2.99 | <.0001 |
| 12–18 months | 0.56    | −0.59 to 1.70 | .3405  |
| 12–24 months | −1.41   | −2.78 to –0.05 | .0422  |
| 18–24 months | −1.97   | −2.92 to –1.02 | <.0001 |

| Prior chemotherapies | LS Mean | 95 % CI      | P value |
|----------------------|---------|--------------|---------|
| Yes                  | 10.99   | 8.20–13.77   | –       |
| No                   | 2.11    | −0.69 to 4.90 | –       |
| Yes–No               | 8.88    | 6.36–11.40   | <.0001  |

| Age group            | LS Mean | 95 % CI      | P value |
|----------------------|---------|--------------|---------|
| >60 years            | 8.04    | 5.04–11.05   | –       |
| ≤60 years            | 5.05    | 2.44–7.66    | –       |
| >60 to ≤60 years     | 2.99    | 0.37–5.61    | .0256   |

| Mastectomy           | LS Mean | 95 % CI      | P value |
|----------------------|---------|--------------|---------|
| Yes                  | 7.63    | 5.88–9.38    | –       |
| No                   | 5.46    | 3.00–7.93    | –       |
| Yes–No               | 2.17    | −2.63 to 6.97 | .3752   |

| Axillary lymph-node dissection | LS Mean | 95 % CI      | P value |
|--------------------------------|---------|--------------|---------|
| Yes                            | 4.77    | 2.00–7.55    | –       |
| No                             | 8.32    | 5.22–11.43   | –       |
| Yes–No                         | −3.55   | −6.68 to −0.41 | .0268  |

CI confidence interval, FACT-B Functional Assessment of Cancer Therapy-Breast, LS least squares, TOI trial outcome index
The mean change in FACT-B SWB was significant at 6 months ($P < .0435$) and 12 months ($P < .0086$) as compared with the baseline value (Table 7). In the MIXED model, baseline TOI, clinical visit, prior chemotherapies, age group, and axillary lymph-node dissection presented statistically significant effects on the FACT-B SWB, whereas mastectomy presented no statistically significant effects on the FACT-B SWB. The LS means of changes from baseline in the FACT-B SWB score with 95% CI are presented in Table 8.

**Discussion**

This first prospective, multicenter, observational, and non-interventional study in Chinese postmenopausal women with HR (+) breast cancer or HR+ EBC undergoing adjuvant treatment with AIs demonstrated significant improvements in the long-term QoL when evaluated at 6, 12, 18, and 24 months post-AI treatment. The study will provide insight to the concerns of the survivors and convey the information to clinical decision-makers who can use it to create patient-centered solutions.

Shen et al. [15] conducted a clinical controlled study in 522 patients to investigate the QoL of Chinese women with breast cancer by using the FACT-B scale. Regression analysis demonstrated that there was a significant increase in FACT-B TOI of the patients >50 years of age, with low-stage cancer, and with high education and income. This was a cross-sectional, single-center observational study in Chinese patients that provided valuable information about factors affecting the QoL of Chinese women with breast cancer. However, dynamic changes on the long-term QoL were not assessed.

Mixed results have been obtained from previous studies conducted on the HRQoL outcomes following AI therapy. Some studies have suggested that treatment with AIs may improve QoL, whereas others have indicated no increased benefit in HRQoL with AI compared with tamoxifen [16]. Fallowfield et al. first published results from a longitudinal follow-up of the impact of 5 years
of adjuvant AI (anastrozole) and tamoxifen (alone/com-
boxination) treatment on HRQoL in a subgroup of 1105
patients (ATAC) [12]. Improvement in TOI was com-
parable in both the treatment groups over the 5-year
recommended adjuvant treatment period [11, 12].

A 5-point increase in the FACT-B TOI is considered
as a significant clinical benefit [17, 18]. The results of our
current analysis are in line with those of the above-
mencitied studies and demonstrated a significant increase
of more than 5 points from baseline (mean: 90.69) to
24 months (mean: 98.72; \( P < .0001 \)), thereby indicating sig-
nificant clinical benefit of adjuvant AIs endocrine therapy
in the QoL of patients with breast cancer.

Kwan et al. [19] demonstrated that the improvement
of FACT-B TOI score in elderly patients (>60 years of
age) was better than that in young patients. In addition,
ATAC study demonstrated improvement of FACT-B
TOI score in patients with previous chemotherapy than
in those with no previous chemotherapy [12]. Our find-
ings are in line with these two studies. The findings
showed significant effects of all of these factors, except
for mastectomy, on the changes in FACT-B TOI scores.

Further exploratory analysis also showed that the TOI
for the previous chemotherapy patient group >60 years
of age without axillary lymph-node dissection was signifi-
cantly improved from the baseline value. Additionally, ef-
fects of baseline score, follow-up, and prior chemotherapy
on changes in FACT-B EWB subscale scores were signifi-
cant, whereas the effects of age group, mastectomy, and
axillary lymph-node dissection were not significant. We
prospectively set the two subscales of FACT-B, i.e. EWB
and SWB as secondary endpoints. We considered that
EWB and SWB are more important to women compared
with other subscales for the breast cancer, as they serve as
an individual resource for dealing with illness and attuning
to uncertainties related with chronic illness. It can also
affect a woman’s self-esteem or may have psychological
impact as a result of breast cancer. There were significant
effects of baseline score, follow-up, previous chemotherapy,
age group, and axillary lymph-node dissection on
changes in FACT-B SWB subscale scores, but mastectomy
had no significant effect. Although studies have analyzed
the HRQoL outcomes following AI treatment, a definitive
comprehensive conclusion on long-term HRQoL is still

| Table 6 | LS mean of changes from baseline in FACT-B EWB score with 95 % CIs (final analysis set) |
|---------|---------------------------------|------------------|-------------|
| Follow-up | 6 months | −0.00 | −0.53 to 0.53 | − |
| 12 months | 0.76 | 0.22−1.30 | − |
| 18 months | 0.92 | 0.36−1.48 | − |
| 24 months | 1.29 | 0.71−1.86 | − |
| 6–12 months | −0.76 | −1.04 to −0.48 | <.0001 |
| 6–18 months | −0.92 | −1.26 to −0.58 | <.0001 |
| 6–24 months | −1.29 | −1.65 to −0.93 | <.0001 |
| 12–18 months | −0.16 | −0.46 to 0.14 | .2895 |
| 12–24 months | −0.53 | −0.88 to −0.18 | .0033 |
| 18–24 months | −0.37 | −0.67 to −0.07 | .0172 |
| Prior chemotherapies | Yes | 1.54 | 0.96−2.12 | − |
| No | −0.06 | −0.64 to 0.53 | − |
| Yes–No | 1.60 | 1.05−2.14 | <.0001 |
| Age group | >60 years | 1.01 | 0.38−1.64 | − |
| ≤60 years | 0.47 | −0.07−1.01 | − |
| >60 years – ≤60 years | 0.54 | −0.03 to 1.10 | .0613 |
| Mastectomy | Yes | 1.20 | 0.85−1.55 | − |
| No | 0.29 | −0.68 to 1.25 | − |
| Yes–No | 0.91 | −0.12 to 1.94 | .0823 |
| Axillary lymph-node dissection | Yes | 0.48 | −0.10 to 1.06 | − |
| No | 1.01 | 0.36−1.65 | − |
| Yes–No | −0.53 | −1.20−0.14 | .1233 |

CI confidence interval, EWB emotional well-being, FACT-B Functional Assessment of Cancer Therapy-Breast, LS least squares
lacking in China. Several unresolved issues still prevent clinicians from designing an optimal endocrine therapy for postmenopausal women with EBC. Thus, the current study provides reinforcement to the previous findings and indicates improved long-term QoL with AI treatment. This will aid clinicians in optimizing treatment to yield effective healthcare outcomes.

Our results were different from those of ATAC and the Intergroup Exemestane Study (IES) substudy, which may be probably because of the following factors: (1) culture background: after treatment, American women with breast cancer were more likely to feel a loss of personal image, intimacy, and sex life than East Asian women [20, 21]; (2) study population: although the patients in ATAC, IES, and this study were menopausal women, there was no clear definition of "menopause" in the relevant published literature; therefore, it cannot be confirmed whether the definition was consistent with that in NCCN-Breast Cancer Version 2013 (having previous bilateral oophorectomy; ≥60 years of age; <60 years of age having experienced amenorrhea for more than 12 months with no chemotherapy, tamoxifen, toremifene, or ovariotomy and follicle-stimulating hormone (FSH) and estradiol within menopausal range; <60 years of age having taken tamoxifen or toremifene, and FSH and plasma estradiol within menopausal range). Women ≤60 years of age accounted for only 33.7 % in the IES study, whereas women ≤60 years of age accounted for 65.0 % in this study.

Finally, the inherent limitations of this study should not be neglected. The study had neither a control or a standard group nor a blinding design. It is well known that a standard endocrine therapy for breast cancer would continue for at least 5 years; however, in the current study, all but 1 patient received the initial hormonal therapy at baseline and the follow-up was only for 2 years. Therefore, the effect of endocrine therapy on 3- to 5-year long-term QoL remains unknown. The aforementioned limitations indicate that this study only recognizes the significant improvements in the long-

| Visit | Clinical efficacy | Final analysis set (N = 486) |
|-------|-------------------|-----------------------------|
|       | Total score       | Change from baseline in total score |
| Baseline | N (missing) | 486 (0) |
| Mean (SD) | 18.61 (6.732) | 0.0–28.0 |
| Median | 19.30 | |
| Min–max | 0.0–28.0 | |
| 6 months | N (missing) | 480 (6) |
| Mean (SD) | 19.14 (6.068) | 0.54 (5.872) |
| Median | 19.83 | 0.00 |
| Min–max | 0.0–28.0 | −24.5 to 28.0 |
| P value in comparison to baseline | .0435 | |
| 12 months | N (missing) | 483 (3) |
| Mean (SD) | 19.35 (6.531) | 0.75 (6.245) |
| Median | 20.00 | 0.00 |
| Min–max | 0.0–28.0 | −21.3 to 28.0 |
| P value in comparison to baseline | .0086 | |
| 18 months | N (missing) | 447 (39) |
| Mean (SD) | 18.32 (6.900) | −0.45 (6.605) |
| Median | 19.00 | 0.00 |
| Min–max | 0.0–28.0 | −20.0 to 28.0 |
| P value in comparison to baseline | 0.1523 | |
| 24 months | N (missing) | 436 (50) |
| Mean (SD) | 18.40 (7.422) | −0.19 (6.961) |
| Median | 19.83 | 0.00 |
| Min–max | 1.0–28.0 | −21.0 to 28.0 |
| P value in comparison to baseline | 0.5677 | |

**Table 7** FACT-B SWB scores at each post-treatment visit and changes from baseline (final analysis set)

**FACT-B** Functional Assessment of Cancer Therapy-Breast, **SD** standard deviation, **SWB** social well-being.
term QoL (6, 12, 18, and 24 months) of postmenopausal Chinese patients with HR+ EBC after starting treatment with AIs and does not provide a robust association between improvement of QoL scores and treatment with AIs. Generally, observational studies have the benefit of assessing multiple aspects of lifestyle and better represent the results; however, potential limitation of selection bias and reporting of scores may have confounded the overall results in this study. We also did not assess the side effects of the treatment by aromatase inhibitors in this population. We had not systematically recorded the safety profile during the study execution and retrospective safety recall would have bias. Taken together, our study results showed the dynamic change of FACT-B, which will guide the physicians to communicate with the HR+ EBC patients about the QOL when receiving adjuvant AIs. Also, the improved QoL will increase patient compliance during the study treatment.

**Conclusions**

The present study demonstrated significant improvements in the long-term QoL of postmenopausal patients with EBC at 6, 12, 18, and 24 months after starting treatment with AIs compared with baseline values. Based on results from the MIXED model (for data collection at 6, 12, and 18 months), we found significant effects of baseline score, follow-up, previous chemotherapy, age group, and axillary lymph-node dissection on changes in FACT-B TOI score and SWB scores, as well as significant effects of baseline score, follow-up, and previous chemotherapy on changes in FACT-B EWB scores. However, there were no significant effects of mastectomy on changes in TOI, SWB, or EWB scores. Further comparative work should be undertaken to strengthen the findings from this study.

**Abbreviations**

AI: Aromatase inhibitor; ATAC: Arimidex, Tamoxifen, Alone or in Combination (trial); BCS: Breast Cancer Subscale; CI: Confidence interval; EBC: Early-age breast cancer; ER+: Estrogen receptor-positive; ES: Endocrine subscale; EWB: Emotional well-being; FACT-B: Functional Assessment of Cancer Therapy-Breast; FACT-G: Functional Assessment of Cancer Therapy-General; FSH: Follicle-stimulating hormone; HR+: Hormone receptor-positive; HRQoL: Health-related QoL; ICF: Informed consent form; IES: Intergroup Exemestane Study; ITT: Intent to treat; LS: Least squares; NCCN: National Comprehensive Cancer Network; PR+: Progesterone receptor-positive; QoL: Quality of life; SD: Standard deviation; SFDA: State Food and Drug Administration; SWB: Social well-being; TOI: Trial outcome index; TNM: Cancer classification system based on tumour (T), lymph node (N) and metastase (M); WHO: World Health Organization.

**Table 8** LS mean of changes from baseline in FACT-B SWB score with 95 % CIs (final analysis set)

| Prior chemotherapies | 6 months | 12 months | 18 months | 24 months |
|----------------------|----------|----------|-----------|-----------|
| Yes                  | 1.75     | 1.30     | -0.19     | 0.06      |
| No                   | -0.64    | -0.19    | -0.99     | -1.02     |
| Yes–No               | 2.40     | 1.50     | 0.33      | 1.05      |

**Table 8** continues...

**Table 8** LS mean of changes from baseline in FACT-B SWB score with 95 % CIs (final analysis set)

| Follow-up | 6 months | 12 months | 18 months | 24 months |
|-----------|----------|-----------|-----------|-----------|
| 6 months  | 0.85     | 1.02      | 0.13      | 0.22      |
| 12 months | 0.85     | 1.02      | 0.13      | 0.22      |
| 18 months | 0.13     | -0.69     | 0.95      | -0.62     |
| 24 months | 0.22     | -0.62     | 1.07      | -0.62     |
| 6–12 months| -0.16    | -0.63     | 0.30      | -0.62     |
| 6–18 months| 0.72     | 0.21      | 1.23      | 0.21      |
| 6–24 months| 0.63     | 0.05      | 1.20      | 0.05      |
| 12–18 months| 0.89     | 0.49      | 1.28      | 0.49      |
| 12–24 months| 0.79     | 0.27      | 1.31      | 0.27      |
| 18–24 months| -0.09    | -0.51     | 0.32      | -0.51     |

**Table 8** continues...

| Age group | 6 months | 12 months | 18 months | 24 months |
|-----------|----------|-----------|-----------|-----------|
| >60 years | 1.30     | 0.39      | -0.99     | -1.02     |
| ≤60 years | 0.22     | 0.68      | -1.16     | -1.16     |
| >60 to ≤60 years | 0.72 | 0.21 | -1.02 | -1.02 |
| Yes       | 0.72     | 0.21      | -1.02     | -1.02     |
| No        | 0.39     | -0.78     | 0.90      | -0.78     |
| Yes–No    | 0.33     | -1.16     | 1.83      | -1.16     |

**Table 8** continues...

| Mastectomy | 6 months | 12 months | 18 months | 24 months |
|------------|----------|-----------|-----------|-----------|
| Yes        | -0.99    | -1.97     | -0.01     | -0.99     |
| No         | 1.05     | 0.10      | 2.00      | 0.10      |
| Yes–No     | -0.99    | -1.97     | -0.01     | -1.97     |

**Table 8** continues...
Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
AC, JZ, XI, WW, YL, ZF, AZ, TZ, DF, JP, HH, LS, XW, YS, DM, and ZS have contributed to study design; acquisition, analysis, and interpretation of data; and drafting and revising the manuscript for important intellectual content. All authors read and approved the final manuscript.

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