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Abemaciclib combined with endocrine therapy as adjuvant treatment for hormone-receptor-positive, HER2–, high-risk early breast cancer: 5-year Chinese population analysis of the phase III randomized monarchE study

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Abstract

Background: Abemaciclib was the first cyclin-dependent kinase 4/6 (CDK4/6) inhibitor approved globally in the adjuvant setting for high-risk hormone-receptor positive (HR+)/human epidermal growth factor 2 negative (HER2–) early breast cancer (EBC), based on the phase III monarchE trial.

Objective: To report an exploratory Chinese population analysis based on the preplanned overall survival (OS) interim analysis with 5-year efficacy results of monarchE.

Design and methods: Patients with HR+/HER2–, high-risk (⩾4 positive lymph nodes, or 1–3 nodes and either tumor size ⩾5 cm, histologic grade 3, or Ki-67 ⩾20%) EBC were randomized (1:1) to abemaciclib (150 mg twice daily for 2 years) plus endocrine therapy (ET), or ET alone. This analysis included Chinese patients enrolled in mainland China, Hong Kong, and Taiwan. The primary endpoint was invasive disease-free survival (IDFS); key secondary endpoints included distant relapse-free survival (DRFS), safety, and patient-reported outcomes (PROs).

Results: Overall, 501 Chinese patients were included (abemaciclib + ET, $n = 259$; ET, $n = 242$). With a median follow-up of 53 months, the addition of abemaciclib to ET resulted in improvements in IDFS (estimated 5-year IDFS rate: 85.9% vs 79.1%; hazard ratio (HR), 0.65 (95% confidence interval (CI) 0.41–1.03)) and DRFS (estimated 5-year DRFS rate: 88.4% vs 82.3%; HR, 0.65 (95% CI, 0.39–1.07)). The most common grade ⩾3 treatment-emergent adverse events in the abemaciclib + ET versus ET groups were neutropenia (24.7% vs 0.8%) and leukopenia (22.4% vs 0.4%). Generally, no clinically meaningful difference in PROs (endocrine symptoms and fatigue) was observed between groups, except for diarrhea.

Conclusion: At this prespecified OS interim analysis, which provides 5-year data, the addition of abemaciclib to ET in Chinese patients with high-risk HR+, HER2– EBC was associated with sustained and clinically meaningful improvements in IDFS and DRFS, with acceptable safety and tolerability profiles and minimal impact on PROs. These results represent the first full report of a CDK4/6 inhibitor in Chinese patients with EBC and support the positive benefit–risk profile of adjuvant abemaciclib + ET in Chinese patients.

Trial registration: ClinicalTrials.gov identifier: NCT03155997 (first posted: May 16, 2017).

Keywords: abemaciclib, adjuvant, breast cancer, Chinese, HR+/HER2–

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Background

In 2020, breast cancer (BC) became the most commonly diagnosed cancer worldwide, with an estimated 2.3 million new cases.[1,2] BC is also the most common cancer in Chinese women, with over 416,000 new cases and over 117,000 deaths estimated in 2020; cases in China account for >18% of all newly diagnosed BC and >16% of all deaths from BC worldwide,[2] representing a large and growing patient population. In addition, BC is typically diagnosed at a younger age in China than in the United States, with the most common age at diagnosis of 45–49 years in China relative to 60–64 years in the United States.[3–6] Therefore, identifying effective treatments for BC in China is an urgent need.

Treatment of hormone-receptor-positive (HR+), human epidermal growth factor 2 negative (HER2−) metastatic BC (MBC) was transformed by cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, such as abemaciclib.[7–9] Successes in advanced HR+/HER2− MBC led to their investigation in the adjuvant setting.[7] Worldwide, abemaciclib was the first CDK4/6 inhibitor to gain regulatory approval (including in China in December 2021) as adjuvant treatment for patients with high-risk HR+/HER2− early BC (EBC). This approval was based on the global phase III monarchE trial (NCT03155997) which, at the second interim analysis, demonstrated that 2 years of adjuvant abemaciclib significantly improved IDFS and DRFS in patients with HR+/HER2− EBC at high risk of recurrence.[10] With longer follow-up, robust and sustained benefits in IDFS and DRFS were observed in the abemaciclib plus endocrine therapy (ET) group.[11]

The most recent pre-specified overall survival (OS) interim analysis (OS IA3) of the global population in monarchE, conducted 3 years after the primary IDFS analysis, demonstrated that the IDFS and DRFS benefits were sustained beyond the completion of treatment (hazard ratio (HR), 0.68 (95% CI, 0.60–0.77) and 0.68 (95% CI, 0.59–0.77), respectively; nominal $p < 0.001$ for both).[12] These were supported by the improvements in 5-year IDFS and DRFS rates of 7.6% and 6.7% for abemaciclib plus ET versus ET alone. OS data were immature; however, fewer deaths occurred in the abemaciclib plus ET group (208, 7.4%) than in the ET group (234, 8.3%).[12]

An earlier exploratory analysis of Chinese patients in monarchE, performed at the primary IDFS analysis, found that abemaciclib plus ET was associated with a clinically meaningful reduction in risk of invasive disease/death and improvements in 2-year IDFS and DRFS.[13] At OS IA2, sustained benefits in IDFS and DRFS were observed in Chinese patients, with clinically meaningful improvements in 4-year IDFS rates and DRFS rates.[14]

Here, at the pre-specified OS IA3, we report results from patients in the monarchE study who were enrolled in Mainland China, Hong Kong, and Taiwan. These data, including 5-year efficacy outcomes, represent the first full report of CDK4/6 inhibition with extended follow-up in Chinese patients with EBC.

Methods

Study design and participants

Detailed methods for the open-label, randomized, phase III monarchE trial have been reported previously.[10,11] Briefly, adults (⩾18 years old) with HR+/HER2−, early-stage, resected, invasive BC without evidence of distant metastases, at high risk of recurrence, were eligible. Patients with ⩾4 positive axillary lymph nodes (ALNs), or 1–3 positive ALNs and either grade 3 disease or tumor ⩾5 cm were enrolled into cohort 1. Patients with involvement of 1–3 ALNs who were deemed high risk based on a high Ki-67 index (Ki-67hi; ⩾20%, assessed centrally) were enrolled into cohort 2.

Patients were randomized (1:1) to receive adjuvant oral abemaciclib (150 mg twice daily) plus standard ET (abemaciclib plus ET group) or standard ET alone. Patients received abemaciclib plus ET or ET for 2 years, with ET planned to continue in both treatment groups for at least 3 and up to 8 years. Randomization was stratified by prior chemotherapy (neoadjuvant/adjuvant/none), menopausal status (pre-/post-menopausal), and region (North America and Europe/Asia/Other).

The study protocol and amendments were approved by local institutional review boards (Supplemental File). The study was conducted in accordance with the Declaration of Helsinki, the Council for International Organizations of Medical Sciences International Ethical Guidelines, and the International Conference on Harmonization Good Clinical Practices Guideline. All patients provided written, informed consent prior to participation.

The reporting of this study conforms to the CONSORT statement (Supplemental File).

Endpoints and assessments

The primary endpoint was IDFS, defined per Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials (STEEP) criteria.[15] Secondary endpoints included DRFS and OS, IDFS in patients with Ki-67hi tumors, safety, and patient-reported outcomes (PROs).

Treatment-emergent adverse events (TEAEs) were recorded during the 2-year treatment period and short-term follow-up (30 days after treatment discontinuation). During long-term follow-up (LTFU), only TEAEs related to study treatment and/or procedures were collected; any-cause serious adverse events (SAEs) were recorded until year 5. Adverse events (AEs) were coded using the Medical Dictionary for Regulatory Activities version 25.0 and their severity was graded according to the Common Terminology Criteria for Adverse Events version 4.0.

Health-related quality-of-life (HRQoL; Functional Assessment of Cancer Therapy (FACT)-Breast (B)), ET-specific symptoms (FACT-ES; including C5 "I have diarrhea"), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)), and symptom burden (FACT-B GP5, "bothered by treatment side effects") were assessed. Detailed methods and assessment schedules are in the Supplemental Appendix.

Statistical analysis

No hypothesis testing or formal statistical analysis was planned for this Chinese population analysis. Prespecified exploratory analyses were conducted among patients enrolled from Mainland China, Hong Kong, and Taiwan. Efficacy analyses were performed in the ITT population using a log-rank test stratified by the randomization factors. The Kaplan–Meier method was used to estimate IDFS and DRFS, and a stratified Cox proportional hazard model (with treatment as a factor) was used to estimate the HR between the treatment arms and corresponding 95% confidence intervals (CIs).

Safety and PROs were analyzed in the safety population, which comprised all randomized patients who received $\geqslant$1 dose of study treatment. For PRO scores, a mixed model for repeated measures was used to compare summary and item scores by treatment arm. For summary scores, an effect size of half the baseline standard deviation was considered a minimally important difference (MID)[16] and for item scores, a change of 1 was considered meaningful.

The data cutoff (DCO) date of this pre-specified analysis was set as July 3, 2023, 3 years after the primary outcome analysis.

Results

Patients

Of the 5637 patients enrolled in monarchE, 501 were Chinese and were included in the Chinese ITT analysis (abemaciclib plus ET, $n=259$; ET, $n=242$). The Chinese safety population included 495 patients (abemaciclib plus ET, $n=259$; ET, $n=236$). All Chinese patients were off treatment at the time of DCO. The 2-year treatment period was completed by 85.6% of patients overall (abemaciclib plus ET, $n=233$ (90.0%); ET, $n=196$ (81.0%); Figure 1). Of Chinese patients, 94.6% entered post-treatment follow-up (abemaciclib plus ET, $n=250$ (96.5%); ET, $n=224$ (92.6%)), and 85.2% were still being followed up at DCO (abemaciclib plus ET, $n=229$ (88.4%); ET, $n=198$ (81.8%); Figure 1). The median duration of follow-up was 53 (interquartile range (IQR), 49.0–56.6) months.

The majority (440/501, 87.8%) of Chinese patients were in cohort 1. Enrollment into cohort 1 began a year before enrollment in cohort 2, which included 61 Chinese patients. Of Chinese patients in cohort 1 (abemaciclib plus ET, $n=224$; ET, $n=216$), 43.0% had Ki-67hi tumors (abemaciclib plus ET, $n=98$; ET, $n=91$) and 36.4% had Ki-67lo tumors (abemaciclib plus ET, $n=87$; ET, $n=73$); 91 (20.7%) Chinese patients had missing, not applicable, or not evaluable Ki-67 results. One Chinese patient in cohort 2 had a missing Ki-67 result.

Baseline characteristics of Chinese patients were similar between the treatment groups in the ITT population (Table 1). All patients were female, with a median age of 46.0 years (range, 23–79), and the majority (62.5%) were premenopausal. Almost all patients had received prior chemotherapy (99.2%), 31.9% as neoadjuvant and 67.3% as adjuvant therapy. Overall, aromatase inhibitors were prescribed as the first on-study ET in 81.6%

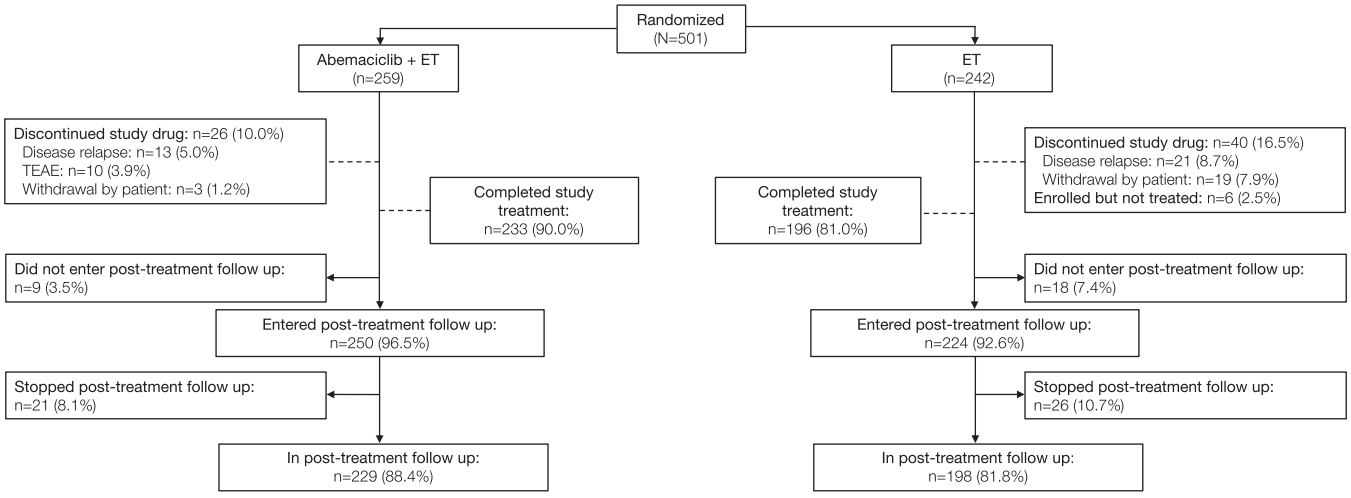

Figure 1. Trial profile in Chinese patients at data cutoff (July 3, 2023).
ET, endocrine therapy; TEAE, treatment-emergent adverse event.

of patients (including 46.5% treated with aromatase inhibitors plus a luteinizing hormone-releasing hormone (LHRH) agonist) and tamoxifen in 15.6% of patients (including 4.4% treated with tamoxifen plus a LHRH agonist). Baseline characteristics for cohort 1 are shown in Supplemental Table S1.

Efficacy

Among Chinese patients, at the time of DCO, 33 IDFS events in the abemaciclib plus ET group (two deaths without invasive disease) and 43 in the ET group (all invasive disease) had occurred. The addition of abemaciclib to ET reduced the risk of invasive disease or death by 34.9% in Chinese patients (HR for IDFS, 0.651 (95% CI, 0.414–1.026); Figure 2). An absolute benefit of 6.8% was observed in the estimated 5-year IDFS rate with abemaciclib plus ET versus ET (85.9% (95% CI, 80.5–89.9) vs 79.1% (95% CI, 72.4–84.4)).

There were 27 DRFS events in Chinese patients in the abemaciclib plus ET group (two deaths without distant relapse) and 36 in the ET group (one death without distant relapse). The addition of abemaciclib to ET resulted in a 35.0% improvement in DRFS (HR for distant relapse/death, 0.650 (95% CI, 0.394–1.071); Figure 3) for Chinese patients. The estimated 5-year DRFS rate was higher with abemaciclib plus ET than ET (88.4% (95% CI, 83.3–92.1) vs 82.3% (95% CI, 75.6–87.3)), an absolute benefit of 6.1%.

IDFS and DRFS benefits were generally similar across the subgroups analyzed, including both premenopausal (IDFS HR, 0.77 (95% CI, 0.41–1.42); DRFS HR, 0.85 (95% CI, 0.43–1.66)) and postmenopausal patients (IDFS HR, 0.55 (95% CI, 0.28–1.08); DRFS HR, 0.46 (95% CI, 0.22–1.00)).

OS data were immature at DCO. There were 14 deaths in the Chinese ITT population; 7 in each treatment group.

Efficacy in Chinese patients in cohort 1 (Supplemental Table S2; Supplemental Figure S1) was consistent with that in the overall Chinese ITT population. The efficacy of abemaciclib plus ET versus ET in Chinese patients was also consistent across patients with Ki-67hi or Ki-67lo (Ki-67 <20%) tumors in cohort 1 (Supplemental Table S2).

Cohort 2 data were immature. Five IDFS (abemaciclib plus ET, $n=2$; ET, $n=3$) and four DRFS events (abemaciclib plus ET, $n=2$; ET, $n=2$) occurred in Chinese patients.

Safety

For Chinese patients, at DCO, the median duration of abemaciclib plus ET was 23.7 months (IQR, 23.6–23.9).

TEAEs in Chinese patients, including TEAEs of interest, are shown in Table 2. At least 1 TEAE was experienced by all 259 patients in the

Table 1. Baseline characteristics of Chinese patients (ITT population).

Characteristic	Abemaciclib plus ET (*n* = 259)	ET alone (*n* = 242)
Age, years, median (range)	46.0 (23–75)	47.0 (25–79)
<65	242 (93.4)	225 (93.0)
⩾65	17 (6.6)	17 (7.0)
Female	259 (100)	242 (100)
ECOG performance status		
0	224 (86.5)	202 (83.8)
1	35 (13.5)	39 (16.2)
Hormone receptor status		
ER positive	258 (99.6)	242 (100)
ER negative	1 (0.4)	0
PR positive	234 (90.3)	214 (88.4)
PR negative	24 (9.3)	28 (11.6)
Menopausal status at diagnosis[a]		
Premenopausal	162 (62.5)	151 (62.4)
Postmenopausal	97 (37.5)	91 (37.6)
Prior chemotherapy		
Neoadjuvant	82 (31.7)	78 (32.2)
Adjuvant	176 (68.0)	161 (66.5)
None	1 (0.4)	3 (1.2)
Positive axillary lymph nodes		
0	0	1 (0.4)
1–3	86 (33.2)	72 (29.8)
⩾4	173 (66.8)	169 (69.8)
Histopathologic grade at diagnosis		
Grade 1	16 (6.2)	6 (2.5)
Grade 2	125 (48.3)	112 (46.3)
Grade 3	84 (32.4)	85 (35.1)
Could not be assessed	27 (10.4)	29 (12.0)

(Continued)

Table 1. (Continued)

Characteristic	Abemaciclib plus ET (*n* = 259)	ET alone (*n* = 242)
Pathologic tumor size		
<2 cm	72 (27.8)	67 (27.7)
2–5 cm	154 (59.5)	131 (54.1)
⩾5 cm	26 (10.0)	31 (12.8)
Ki-67 index		
Low (<20%)	87 (33.6)	73 (30.2)
High (⩾20%)	133 (51.4)	116 (47.9)
Not evaluable	9 (3.5)	13 (5.4)
TNM stage (derived)[b]		
IIA	30 (11.6)	28 (11.6)
IIB	33 (12.7)	21 (8.7)
IIIA	96 (37.1)	102 (42.1)
IIIB	7 (2.7)	3 (1.2)
IIIC	88 (34.0)	84 (34.7)
Received prior adjuvant chemotherapy	201 (77.6)	185 (76.4)
Time from surgery to randomization, median (IQR) months	8.1 (6.0–9.1)	8.0 (5.8–9.0)
First on-study ET[c]		
Tamoxifen	40 (15.4)	37 (15.7)
Plus LHRH agonist (any time)	8 (3.1)	14 (5.9)
Toremifene	5 (1.9)	9 (3.8)
Aromatase inhibitors	214 (82.6)	190 (80.5)
Plus LHRH agonist (any time)	125 (48.3)	105 (44.5)
Letrozole	114 (44.0)	99 (41.9)
Exemestane	62 (23.9)	49 (20.8)
Anastrozole	38 (14.7)	42 (17.8)
LHRH agonist (any time)[c]	137 (52.9)	127 (53.8)

Data are *n* for non-missing data (%) unless otherwise specified.
[a]Based on IWRS data.
[b]Based on pathologic tumor size and the number of positive lymph nodes.
[c]Data available for 236 patients in the ET alone group.
ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; ET, endocrine therapy; IQR, interquartile range; ITT, intention to treat; IWRS, interactive web-response system; LHRH, luteinizing hormone-releasing hormone; NA, not available; PR, progesterone receptor; TNM, tumor, node, metastasis.

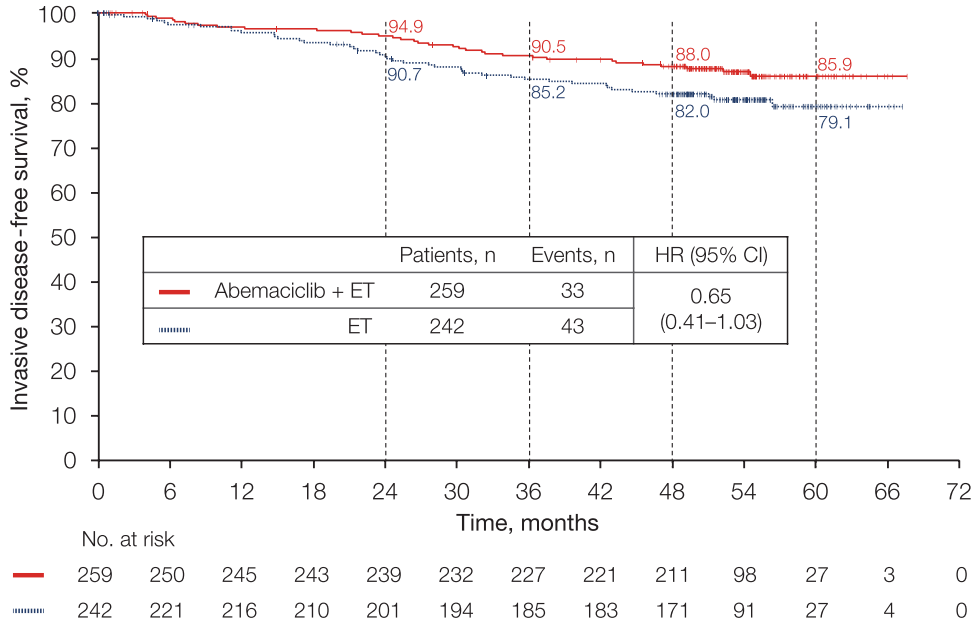

Figure 2. IDFS in Chinese patients (*N* = 501).
CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IDFS, invasive disease-free survival.

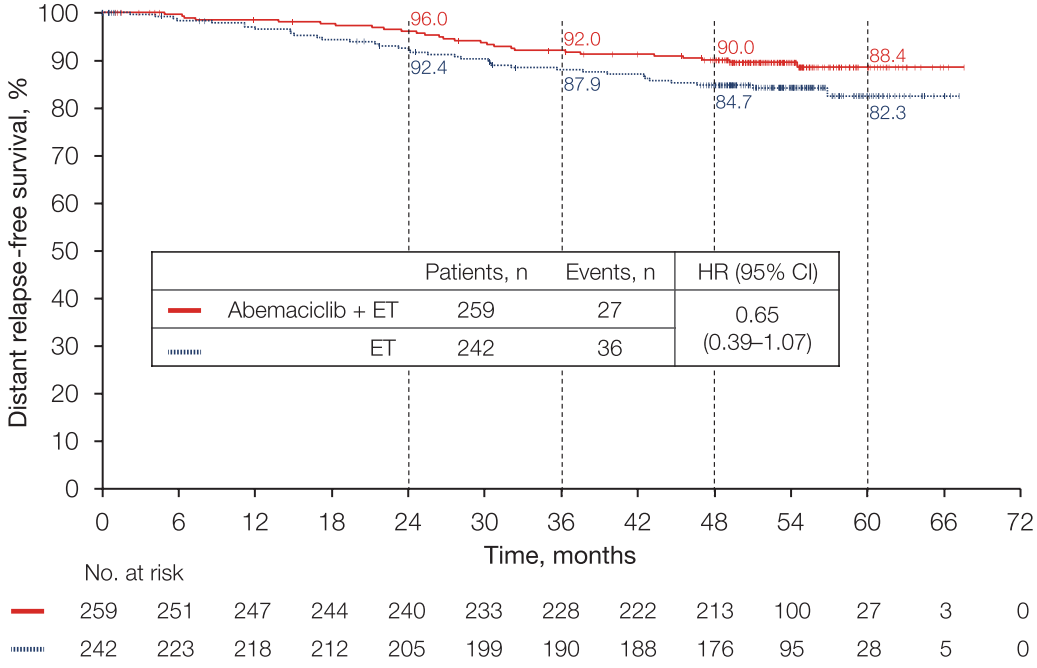

Figure 3. DRFS in Chinese patients (*N* = 501).
CI, confidence interval; DRFS, distant relapse-free survival; ET, endocrine therapy; HR, hazard ratio.

abemaciclib plus ET group and by 215 (91.1%) in the ET group. Of these patients, 142 (54.8%) and 32 (13.6%) experienced grade ⩾3 TEAEs in the abemaciclib plus ET and ET groups, respectively; the most common grade ⩾3 TEAEs in the abemaciclib plus ET versus ET groups were neutropenia (24.7% vs 0.8%) and leukopenia (22.4% vs 0.4%). In the abemaciclib plus ET group, pulmonary embolism was reported in one patient (0.4%) and deep-vein thrombosis was reported in

Table 2. Summary of TEAEs (Chinese safety population).

AE	Abemaciclib plus ET (*n* = 259)		ET alone (*n* = 236)	
⩾1 TEAE	259 (100)		215 (91.1)	
⩾1 CTCAE Grade ⩾3 TEAE	142 (54.8)		32 (13.6)	
⩾1 SAE	44 (17.0)		24 (10.2)	
TEAE leading to treatment discontinuation	10 (3.9)		0 (0)	
SAE leading to treatment discontinuation	0 (0)		0 (0)	
Death due to AE on treatment or within 30 days of treatment discontinuation	0 (0)		0 (0)	
TEAEs in ⩾10% of patients in either treatment group	Any grade	Grade ⩾3	Any grade	Grade ⩾3
Diarrhea	239 (92.3)	15 (5.8)	17 (7.2)	0
Neutropenia	200 (77.2)	64 (24.7)	31 (13.1)	2 (0.8)
Leukopenia	200 (77.2)	58 (22.4)	43 (18.2)	1 (0.4)
Anemia	95 (36.7)	3 (1.2)	12 (5.1)	0
Upper respiratory tract infection	90 (34.7)	1 (0.4)	66 (28.0)	0
AST increased	89 (34.4)	11 (4.2)	30 (12.7)	2 (0.8)
ALT increased	83 (32.0)	17 (6.6)	36 (15.3)	1 (0.4)
Thrombocytopenia	76 (29.3)	7 (2.7)	9 (3.8)	0
Abdominal pain	66 (25.5)	3 (1.2)	20 (8.5)	0
Insomnia	48 (18.5)	0	35 (14.8)	0
Fatigue	47 (18.1)	1 (0.4)	22 (9.3)	0
Hot flush	44 (17.0)	0	37 (15.7)	0
Pyrexia	43 (16.6)	1 (0.4)	18 (7.6)	0
Arthralgia	40 (15.4)	0	68 (28.8)	0
Dizziness	40 (15.4)	2 (0.8)	21 (8.9)	0
Headache	39 (15.1)	0	22 (9.3)	0
Lymphopenia	37 (14.3)	14 (5.4)	7 (3.0)	0
Cough	36 (13.9)	0	19 (8.1)	0
Nausea	33 (12.7)	2 (0.8)	7 (3.0)	0
Vomiting	33 (12.7)	2 (0.8)	6 (2.5)	0
Pruritus	29 (11.2)	0	17 (7.2)	0
Rash	30 (11.6)	0	18 (7.6)	0
Osteoporosis	14 (5.4)	0	24 (10.2)	0

(Continued)

Table 2. (Continued)

AE	Abemaciclib plus ET (*n* = 259)		ET alone (*n* = 236)	
Other TEAEs of interest	Any grade	Grade ⩾3	Any grade	Grade ⩾3
Infection[a]	142 (54.8)	16 (6.2)	103 (43.6)	10 (4.2)
Venous thromboembolic events	3 (1.2)	2 (0.8)	0	0
DVT[b]	2 (0.8)	1 (0.4)	0	0
Pulmonary embolism	1 (0.4)	1 (0.4)	0	0
Pneumonitis	16 (6.2)	0	6 (2.5)	0
Interstitial lung disease	1 (0.4)	0	0	0

[a]Includes all preferred terms under the MedDRA SOC, "Infections and Infestations."
[b]Includes jugular vein thrombosis and venous thrombosis limb.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; DVT, deep-vein thrombosis; ET, endocrine therapy; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SOC, System Organ Class; TEAE, treatment-emergent adverse event.

two patients (0.8%). Ten patients (3.9%) in the abemaciclib plus ET group discontinued the study treatment period due to TEAEs, none of which was an SAE. All deaths occurred >30 days after treatment discontinuation and none occurred during treatment. Of the seven patients in the abemaciclib plus ET group who died, three (1.2%) died due to an AE. One of these deaths (acute kidney injury) was considered related to treatment. In the ET group, one (0.4%) patient died due to an AE (cervical carcinoma), which was not considered related to ET.

During LTFU, 70/250 Chinese patients (28.0%) in the abemaciclib plus ET group and 42/222 (18.9%) in the ET group experienced a treatment-related AE. In total, 15 (6.0%) patients in the abemaciclib plus ET group and 19 (8.6%) in the ET group experienced an SAE (regardless of causality) during LTFU. Differences between treatment groups in the incidence of treatment-related AEs were mainly in laboratory values (none of which were grade ⩾3), such as alanine aminotransferase (ALT) increased (9.2% vs 1.4%), aspartate aminotransferase (AST) increased (6.0% vs 2.3%), blood alkaline phosphatase increased (3.2% vs 0.5%); leukopenia also occurred in 4.4% versus 1.8% of patients, respectively (the only grade ⩾3 leukopenia event was in one (0.4%) patient in the abemaciclib plus ET group). Three (1.2%) patients in the abemaciclib plus ET group experienced treatment-related diarrhea (none grade ⩾3).

Patient-reported outcomes

Changes in FACT-B summary scores were less than the MID (Supplemental Table S3). There was no clinically meaningful difference in patient-reported endocrine symptoms and fatigue between treatment groups, with changes less than the MID for summary scores for FACT-ES (ESS19 subscale) and FACIT-F instruments in both groups (Supplemental Table S3). During treatment, more patients in the abemaciclib plus ET group reported diarrhea (FACT-ES C5) than in the ET group; however, the majority of these patients reported having diarrhea "a little bit" or "somewhat." During follow-up, the frequency of patient-reported diarrhea reduced after abemaciclib discontinuation (Supplemental Figure S2). Changes from baseline in FACT-B GP5 were less than the MID of 1 in both groups. The majority of patients in both groups reported being bothered by side effects "a little" or "not at all" (Supplemental Figure S3).

Discussion

This prespecified OS interim analysis of monarchE, including 5-year efficacy outcomes, indicated that the addition of abemaciclib to ET for high-risk HR+, HER2− EBC resulted in IDFS and DRFS improvements in Chinese patients, with no new safety signals and a minimal impact on HRQoL. Our data complement results from both the global population and Chinese

patients from previous analyses that established the benefits of abemaciclib plus ET in IDFS and DRFS,[10–13,17] and represent the first full report of a CDK4/6 inhibitor in Chinese patients with EBC at high risk of disease recurrence at the pivotal 5-year milestone.

These updated data show sustained efficacy of abemaciclib plus ET in both Chinese patients and the global population in monarchE at longer durations of follow-up.[10,12,13] Previous data have shown clinically meaningful IDFS and DRFS benefits in Chinese patients with abemaciclib plus ET versus ET.[13] Additional analyses with longer durations of follow-up (including analyses of 5-year efficacy outcomes) continue to demonstrate clinically meaningful benefits of abemaciclib plus ET in both IDFS and DRFS, sustained beyond the 2-year abemaciclib treatment period.[12,17] These most recent data in Chinese patients, allowing assessment of 5-year efficacy outcomes, confirm the benefit initially observed.

Young age and premenopausal status are associated with worse survival among patients with HR+/HER2− BC,[18–21] and biological differences have been observed in Asian patients with HR+/HER2− BC.[22,23] In this analysis of Chinese patients, which included mostly (62.5%) premenopausal patients, a benefit in IDFS with abemaciclib plus ET was observed in both premenopausal and postmenopausal patients, with DRFS showing similar trends. This is consistent with the observation of clinical benefit regardless of menopausal status in the global population.[17]

The efficacy in Chinese patients in cohort 1 and the overall Chinese ITT population was consistent, which was expected, as the majority of patients in the ITT population were in cohort 1. Ki-67 is an important marker of cell division and a valuable prognostic biomarker for HR+ HER2− BC.[24] Notably, in Chinese patients in cohort 1, numerical improvements in both IDFS and DRFS with abemaciclib plus ET were observed regardless of high (⩾20%) or low (<20%) Ki-67 index. Data from cohort 2 ($n=61$) were immature. Longer follow-up will aid further analysis of the cohort.

The safety profile of abemaciclib plus ET in Chinese patients remained consistent with the established and manageable safety profile in global and previous Chinese reports, with no new safety signals during longer follow-ups.[11–13,17] The proportion of Chinese patients who experienced SAEs during LTFU was lower in the abemaciclib plus ET group (6.0%) than in the ET group (8.6%). The proportion of Chinese patients in the abemaciclib plus ET arm who discontinued treatment due to AEs (3.9%) was consistent with the global population (6.4%), suggesting that most of these AEs were manageable in Chinese patients.

The HRQoL results support the manageable safety profile in Chinese patients. Changes from baseline in HRQoL summary scores, as assessed by FACT-B and FACT-ES, were generally less than the MID. Notably, in the one scale where a clinically meaningful difference from baseline was reported (diarrhea), this was usually mild. The majority of patients' diarrhea had resolved in the follow-up visits after treatment cessation (a severity of "0" after the 2-year treatment period), highlighting that this was manageable and reversible, consistent with prior reports in the global population.[25]

Limitations of this analysis include the limited sample size (and a corresponding number of events); this population included 501 of the total 5637 patients included in monarchE. By definition, post hoc population analyses are not alpha-controlled and no formal statistical analyses can be made. While the small sample size resulted in wider CIs for HRs, it is notable that clinically meaningful benefits were still observed for the primary IDFS endpoint and the key secondary DRFS endpoint. In addition, OS data were not mature at this DCO, precluding formal analysis; further follow-up is required and ongoing to clarify the impact of adjuvant abemaciclib plus ET on OS in Chinese patients.

Conclusion

The addition of abemaciclib to ET in Chinese patients with high-risk HR+, HER2− EBC resulted in clinically meaningful improvements in IDFS and DRFS that are sustained beyond the 2-year abemaciclib treatment period, with no new safety signals observed and a minimal impact on HRQoL. These updated results further clarify the effects of abemaciclib plus ET in this setting and support the positive benefit–risk profile of abemaciclib plus ET in Chinese patients.

Declarations

Ethics approval and consent to participate

The study protocol and amendments were approved by local institutional review boards. The study was conducted in accordance with the Declaration of Helsinki, the Council for International Organizations of Medical Sciences International Ethical Guidelines, and the International Conference on Harmonization Good Clinical Practices Guideline. All patients provided written, informed consent prior to participation.

Consent for publication

Not applicable.

Author contributions

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Competing interests

L.Y. and C.Q. are employees of Eli Lilly and Company. The other authors declare they have no competing interests.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Supplemental material

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