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Clinical efficacy of palbociclib-based therapy in women with HR+/HER2- metastatic breast cancer in the real-world setting for Chinese women: a comparison with the IRIS study

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Abstract. – OBJECTIVE: This retrospective study aimed to explore the clinical efficacy of palbociclib with endocrine therapy (ET) in women with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer in real-world practice.

PATIENTS AND METHODS: This retrospective study analyzed the medical records of patients to determine treatment outcomes. Progression-free survival (PFS) curves were generated using log-rank tests with the Kaplan-Meier method. Treatment outcomes in Chinese patients were compared with those in patients from the USA, Argentina, Canada, and Europe in the IRIS study.

RESULTS: In total, 69 patients were included in this study. The median PFS was 12.8 months (95% confidence interval: 10.1-15.5). A longer PFS was observed for patients with bone-only metastases, no liver metastases, no previous palliative chemotherapy, no previous palliative ET, and ET sensitivity. The overall response rate was 10.1%, and the clinical benefit rate was 78.3%. Nineteen patients (27.5%) received a reduced dose of palbociclib according to the decision of their physicians. Dose reduction did not affect the clinical efficacy of the combined treatment. Compared with those in the IRIS study, Chinese patients receiving palbociclib-based treatment were younger, and they had fewer bone-only metastases and more visceral and liver metastases. The clinical benefit rate and overall response rate for Chinese patients were lower than those observed for the patients in the IRIS study.

CONCLUSIONS: ET combined with palbociclib treatment was effective and well-tolerated in HR+/HER2- metastatic breast cancer patients in the real-world setting. Earlier use of palbociclib-ET was associated with more clinical benefits in HR+/HER2- metastatic breast cancer.

Key Words:
Palbociclib, Endocrine therapy, Clinical efficacy, Metastatic breast cancer, IRIS study.

Introduction

Breast cancer (BC) is the most commonly diagnosed cancer in women. It can generally be classified into three subtypes: hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative BC (HR+/HER2- BC), HER2-positive BC, and triple-negative BC[1]. HR+/HER2- BC accounts for approximately 70% of all BC cases[2]. In the past decades, treatments of HR+/HER2- BC focus on mainly blocking the estrogen receptor (ER) signaling pathway. The endocrine therapy (ET) was the standard of care for women with HR+/HER2- BC[3]. With the discovery of cyclin-dependent kinase (CDK) 4/6 inhibitors, progression-free survival (PFS) was significantly prolonged with the combination of CDK4/6 inhibitors and ET in patients with HR+/HER2- metastatic BC (MBC)[4].

Palbociclib is an oral CDK4/6 inhibitor that blocks cell cycle progression from the G_1 phase to S phase[5]. It reduces the proliferation of BC cells by inhibiting phosphorylation of retino-

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blastoma protein[5]. Two phase III randomized clinical trials, PALOMA-2 and PALOMA-3 have demonstrated the clinical effectiveness and safety of palbociclib in HR+/HER2- advanced BC (ABC)/MBC[6,7]. In combination with letrozole, palbociclib extended the PFS from 14.5 months to 27.6 months (hazard ratio: 0.563; $p < 0.001$)[6] in treatment-naïve patients with HR+/HER2- ABC/MBC[6]. When combined with fulvestrant in previously treated patients with HR+/HER2- ABC/MBC, PFS was prolonged from 4.6 months to 9.5 months (hazard ratio: 0.46; $p < 0.001$) in palbociclib plus fulvestrant arm[7]. In premenopausal patients, the Young-PEARL study indicated that palbociclib plus exemestane with ovarian function suppression (leuprolide) prolongs PFS to 20.1 months compared with a PFS of 14.4 months (hazard ratio: 0.659; $p = 0.0235$) in the capecitabine group in premenopausal women with HR+/HER2- MBC[8]. These results support the use of palbociclib plus ET as a promising approach in patients with HR+/HER2- MBC[9].

The multicountry Ibrance Real World Insights (IRIS) study is a retrospective chart review exploring the treatment patterns and clinical outcomes among patients receiving palbociclib combined with ET for HR+/HER2- ABC/MBC in real-world clinical practice[10]. This study included patients from multiple countries in North America, South America, and Europe[11]. To date, real-world data from the USA, Argentina, Canada, and Europe (non-Chinese countries) have been published[10-13]. The patients included in clinical trials strictly met all inclusion and exclusion criteria and had received standard treatment. However, patient characteristics are uncontrolled in clinical practice compared with clinical trials. Therefore, comparison with the IRIS study could provide insights into the clinical efficacy of palbociclib among various patients.

In China, palbociclib was approved by the National Medical Products Administration on July 31, 2018. Within the last two years, many women with HR+/HER2- ABC/MBC have benefitted from palbociclib-based therapy. Accordingly, this study aimed to share the real-world experience on the use of palbociclib combined with ET in order to provide evidence for the clinical use of palbociclib in China. The treatment outcomes in Chinese patients from this study were compared with those in patients from the non-Chinese countries reported in the IRIS study.

Patients and Methods

Study Population

This study was approved by the Ethics Committee of Ruijin Hospital Shanghai Jiaotong University School of Medicine and was conducted according to the principles of the Declaration of Helsinki. Because of the nature of this retrospective study, in which patient privacy and personal information were protected, the ethics committee waived the requirement to obtain informed consent.

In this retrospective observational cohort study, 69 patients with BC were enrolled from two centers in China, Ruijin Hospital Shanghai Jiaotong University School of Medicine and the First Affiliated Hospital of Soochow University. The patients were enrolled between March 1, 2018 and April 30, 2020. Eligible patients met the following criteria: HR-positive (ER or progesterone receptor)/HER2-negative BC confirmed by histological examination, uncurable metastatic disease treated with palbociclib plus ET (tamoxifen, aromatase inhibitors [AIs], or fulvestrant), and Eastern Cooperative Oncology Group performance status of 0-3. Patients with brain metastases were also included. HR-positive/HER2-negative BC was defined as follows: HR (> 1% ER) positive plus HER2 negative (immunohistochemistry score = 0-1) or negative based on the fluorescence in situ hybridization ratio[14], indicative of a luminal A or luminal B (HER2-negative) subtype according to 2011 St. Gallen international Breast Cancer Conference[15].

The disease response to palbociclib plus ET was evaluated using Response Evaluation Criteria In Solid Tumors version 1.1 (https://recist.eortc.org/recist-1-1-2/)[16]. Adverse events were recorded and graded according to the Common Terminology Criteria for Adverse Events version 4.03 (https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/).

Treatment

Enrolled patients received palbociclib (Pfizer, New York, NY, USA) at a starting dose of 125 mg/day on a 3/1 schedule (21 days on, 7 days off). The combined ET was selected by the physicians and included AIs, fulvestrant (AstraZeneca, Cambridge, UK), or tamoxifen (20 mg/day, Forwardpharm, Shanghai, China) until disease progression, intolerable toxicity, or death. AIs prescribed in this study were letrozole (2.5 mg/day Novartis, Basel, Swiss), anastrozole (1 mg/day, AstraZeneca), or exemestane (25 mg/day,

Pfizer). Fulvestrant (500 mg) were injected intramuscular 500 mg by intramuscular injection on days 1 and 15 of the first cycle and on day 1 of subsequent cycles every 28 days. Premenopausal patients were under ovarian function suppression with goserelin (3.6 mg administered subcutaneously on day 1 of every 28-day cycle, AstraZeneca). Dose delay or dose reduction of palbociclib was allowed according to the prescribing instructions. Tumor assessments were performed using computed tomography (Siemens, Munich, Germany) or magnetic resonance imaging (GE, Boston, MA, USA) at screening every 8 or 12 weeks (according to the decision of the physicians) until disease progression. PFS was defined as the time from beginning ET and palbociclib therapy to disease progression or patient death.

Statistical Analysis

All statistical analyses were conducted using SPSS 19 (IBM, Armonk, NY, USA). Proportions were presented as crude numbers and percentages. PFS was evaluated using log-rank tests with the Kaplan-Meier method. Differences in PFS between groups (metastatic site, line of therapy, and sensitivity to ET) were also evaluated. Hazard ratios with 95% confidence intervals (CIs) were reported. Results with *p*-values less than 0.05 were considered statistically significant. The data cut-off date was April 30, 2020.

Results

Patient Characteristics

This study included 69 patients with HR+/HER2- MBC treated with palbociclib plus ET. Until the time of data cut-off, 38 patients (55%) were still receiving treatment with palbociclib plus ET, and 31 (45%) patients had discontinued palbociclib-based treatment due to disease progression. The clinical characteristics of the patients are shown in Table I. The definition of endocrine sensitivity was in compliance with the ESO-ESMO 2nd International Consensus Guidelines for Advanced Breast Cancer[17]. Primary endocrine resistance was defined as follows: a relapse while on the first 2 years of adjuvant ET, or progressive disease (PD) within first 6 months of first-line ET for MBC, while on ET. Secondary endocrine resistance was defined as follows: a relapse while on adjuvant ET but after the first 2 years, or a relapse within 12 months of completing adjuvant ET, or PD ≥ 6 months after initiating ET for MBC, while on ET.

Among all patients, the mean age was 56.4 ± 12.5 years. Additionally, 50 (72.5%) of the patients were premenopausal, and 19 (27.5%) were postmenopausal. Premenopausal patients were co-prescribed goserelin plus palbociclib and ET. Twenty-one (30.4%) patients were diagnosed with *de novo* stage IV BC. The number of patients with visceral disease was 39 (56.5%), and 24 of these patients had liver metastases. There were 12 (17.4%) patients with bone-only metastases. Regarding progestogen receptor status, 48 (69.6%) of the 69 patients were progestogen receptor positive, and 21 (30.4%) of them were progestogen receptor negative. Moreover, 32 (46.4%) patients had received previous ET for MBC. Twenty (29.0%) patients had previously received chemotherapy for MBC, and 34 (49.3%) patients did not receive any systemic treatment for MBC. In contrast, 21 (30.4%) patients received palbociclib as the 3+ line of treatment. Twenty (29.0%) patients were sensitive to ET, 36 (52.2%) showed primary resistance to ET, and 13 (18.8%) showed secondary resistance to ET. Only one (1.5%) patient was given palbociclib and tamoxifen, 39 (56.5%) patients were given palbociclib and AI (letrozole, n = 25; exemestane, n = 10; anastrozole, n = 4), and 29 (42%) patients were given palbociclib and fulvestrant.

In comparison to the patients in the IRIS study (Table I), the Chinese patients included in this study were younger than the non-Chinese patients. There were more visceral and liver metastases in the Chinese patients than in the non-Chinese patients. Most patients in this study were premenopausal women, which was opposite to the trend observed in the IRIS study. There was a higher proportion of Chinese patients who received prior chemotherapy or ET in this study as compared to the proportion in the IRIS study. Additionally, the Chinese patients were much more heavily pretreated (≥ 3 lines of treatment) than the non-Chinese patients.

Clinical Efficacy

All 69 patients received the first radiological assessments at 8 or 12 weeks after treatment with palbociclib (Table II). Seven (10.1%) patients showed a partial response (PR), and no patients achieved complete response (CR). The overall response rate (ORR) was 10.1%. 47 (68.2%) patients

Table I. Patients characteristics.

Variables	China, n (%)	IRIS study (non-Chinese countries)			
		USA, n (%)	Argentina, n (%)	Canada, n (%)	Europe, n (%)
Age, Mean (SD)	56.4 (12.5)	64.0 (10.9)	64 (10)	61.9 (10.2)	62.8 (10.8)
Menopausal status					
Premenopausal	50 (72.5)	82 (12.6)	15 (9.3)	23 (9.3)	–
Postmenopausal	19 (27.5)	570 (87.4)	145 (89.5)	224 (90.7)	–
ECOG PS					
0-1	54 (78.3)	539 (82.7)	143 (88.3)	200 (81.0)	892 (87.7)
2-3	15 (21.7)	113 (17.3)	19 (11.7)	47 (19.0)	81 (8.0)
De novo stage IV					
Yes	21 (30.4)	285 (43.7)	63 (38.9)	158 (64.0)	441 (43.4)
No	48 (69.6)	367 (56.3)	99 (61.1)	89 (36.0)	576 (56.6)
Visceral metastasis					
Yes	39 (56.5)	240 (46.4)	–	119 (58.3)	436 (47.9)
No	30 (43.5)	277 (53.6)	–	85 (41.7)	475 (52.1)
Liver metastasis					
Yes	24 (34.8)	–	28 (17.2)	43 (21.1)	–
No	45 (65.2)	–	134 (82.7)	161 (78.9)	–
Bone-only					
Yes	12 (17.4)	240 (46.4)	–	–	361 (39.6)
No	57 (82.6)	277 (53.6)	–	–	550 (60.4)
Progesterone Receptor status					
Positive	48 (69.6)	–	–	–	–
Negative	21 (30.4)	–	–	–	–
Prior endocrine therapy for MBC					
Yes	32 (46.4)	153 (23.5)	40 (24.7)	20 (8.1)	–
No	37 (53.6)	499 (76.5)	122 (75.3)	227 (91.9)	–
Prior chemotherapy for MBC					
Yes	20 (29.0)	43 (7.6)	12 (7.4)	11 (4.5)	–
No	49 (71.0)	609 (93.4)	150 (92.6)	236 (95.5)	–
Lines of treatment for MBC					
1	34 (49.3)	376 (57.7)	105 (64.8)	204 (82.6)	841 (82.7)
2	14 (20.3)	227 (34.8)	50 (30.9)	34 (13.8)	157 (15.4)
≥ 3	21 (30.4)	49 (7.5)	7 (4.3)	9 (3.6)	19 (1.9)
Endocrine sensitivity					
Sensitive	20 (29.0)	–	–	–	–
Primary resistant	36 (52.2)	–	–	–	–
Secondary resistant	13 (18.8)	–	–	–	–
Endocrine agent companion					
Tamoxifen	1 (1.5)	0	0	0	0
AI	39 (56.5)	360 (55.2)	105 (64.8)	214 (86.6)	582 (57.2)
Fulvestrant	29 (42.0)	292 (44.8)	57 (35.2)	33 (13.4)	435 (42.8)

[a]Radiological response to the first assessment; [b]Where 'complete response' and 'partial response' has been recorded at any time on treatment (no 24-week minimum).

Table II. Radiological response to palbociclib-based treatment.

	China[a], n (%)	IRIS study[b] (non-Chinese countries)			
		USA, n (%)	Argentina, n (%)	Canada, n (%)	Europe, n (%)
Clinical benefit rate	54 (78.3)	596 (93.6)	148 (94)	231 (93.9)	846 (83.8)
Overall response rate	7 (10.1)	491 (75.3)	105 (66)	197 (80.1)	819 (80.5)
Complete response	0 (0)	63 (9.9)	10 (6)	26 (10.6)	180 (17.7)
Partial response	7 (10.1)	428 (67.2)	95 (60)	171 (69.5)	639 (62.8)
Stable disease	47 (68.2)	96 (15.1)	48 (30)	33 (13.4)	145 (14.3)
Disease Progression	15 (21.7)	65 (10.0)	5 (3)	12 (4.9)	18 (1.8)

[a]Radiological response to the first assessment; [b]Where 'complete response' and 'partial response' has been recorded at any time on treatment (no 24-week minimum).

had stable disease and 15 (21.7%) showed disease progression. The clinical benefit rate (CBR) was 78.3%. The CBR and ORR were lower in Chinese patients than those in the patients in the IRIS study. More Chinese patients experienced stable disease and disease progression than the patients in the IRIS study.

The median PFS in the overall population and subgroups is listed in Table III. In the overall population, the median PFS was 12.8 months (95% CI: 10.1-15.5; Figure 1A). The median PFS was 15.4 months (95% CI: 12.2-18.5) in patients with bone-only metastases. This was longer than that in patients without bone-only metastases (11.4 months; 95% CI: 8.5-14.2; $p = 0.026$; Figure 1B). There were no significant differences in median PFS between the visceral and non-visceral groups (11.9 months [95% CI: 8.3-15.6] *vs.* 11.8 months [95% CI: 9.4-14.3], respectively; $p = 0.176$; Figure 1C). Patients with liver metastases had a shorter PFS than that of the patients without liver metastases (8.9 months [95% CI: 5.0–12.8] *vs.* 12.7 months [95% CI: 10.4-15.0], respectively; $p = 0.004$; Figure 1D).

The median PFS was 17.2 months (95% CI: 10.8-16.0) for patients receiving palbociclib and ET as first-line treatment for MBC (Figure 2A). This was longer than that of the patients who had received palbociclib and ET as second-line treatment (8.6 months; 95% CI: 5.3-9.5, $p = 0.001$) and third-line treatment (11.8 months; 95% CI: 5.1-16.9, $p = 0.006$) for MBC (Figure 2A). No significant differences were observed between the results of the second-line and third-line treatments for MBC ($p = 0.87$, Figure 2A). Patients who had received prior chemotherapy had a poorer prognosis than those who did not receive prior chemotherapy (8.9 months [95% CI: 4.8-12.9] *vs.* 12.4 months [95% CI: 10.0-14.7], respectively; $p = 0.0146$; Figure 2B). ET-sensitive patients had a longer median PFS (15.9 months; 95% CI: 12.3-19.4) than the patients with primary resistance to ET (PFS: 9.2 months; 95% CI: 6.2-12.1; $p = 0.005$) and secondary resistance to ET (PFS: 5.4 months; 95% CI: 2.4-8.4; $p = 0.16$; Figure 2C). There were no significant differences between the patients with primary and secondary resistance to ET ($p = 0.188$).

Tolerability

All Chinese patients in this study started palbociclib treatment at 125 mg/day. 19 (27.5%) patients have experienced dose reduction according to the decision of the physicians (Ta-

Table III. Progression-free survival in Chinese patients.

	Median PFS (months)	95% CI	*p*-value
Overall	12.8	10.1-11.5	
Visceral metastasis			
Yes	11.9	8.3-15.6	0.176
No	11.8	9.4-14.3	
Liver metastasis			
Yes	8.9	5.0-12.8	0.004
No	12.7	10.4-15.0	
Bone-only			
Yes	15.4	12.2-18.5	0.026
No	11.4	8.5-14.2	
Lines of treatment			
1	17.2	10.8-16.0	
2	8.6	5.3-9.5	0.001[a]
3	11.8	5.1-16.9	0.006[b]
Prior chemotherapy			
Yes	8.9	4.8-12.9	0.015
No	12.4	10.0-14.7	
Endocrine sensitivity			
Sensitive	15.9	12.3-19.4	
Primary resistant	9.2	6.2-12.1	0.005[c]
Secondary resistant	5.4	2.4-8.4	0.16[d]
Dose reduction			
Yes	10.2	6.2-14.1	0.332
No	13.3	10.2-16.3	

Note: [a]$p = 0.001$ versus (*vs.*) first-line treatment; [b]$p = 0.006$ *vs.* first-line treatment; [c]$p = 0.005$ *vs.* sensitive; [d]$p = 0.16$ *vs.* sensitive.

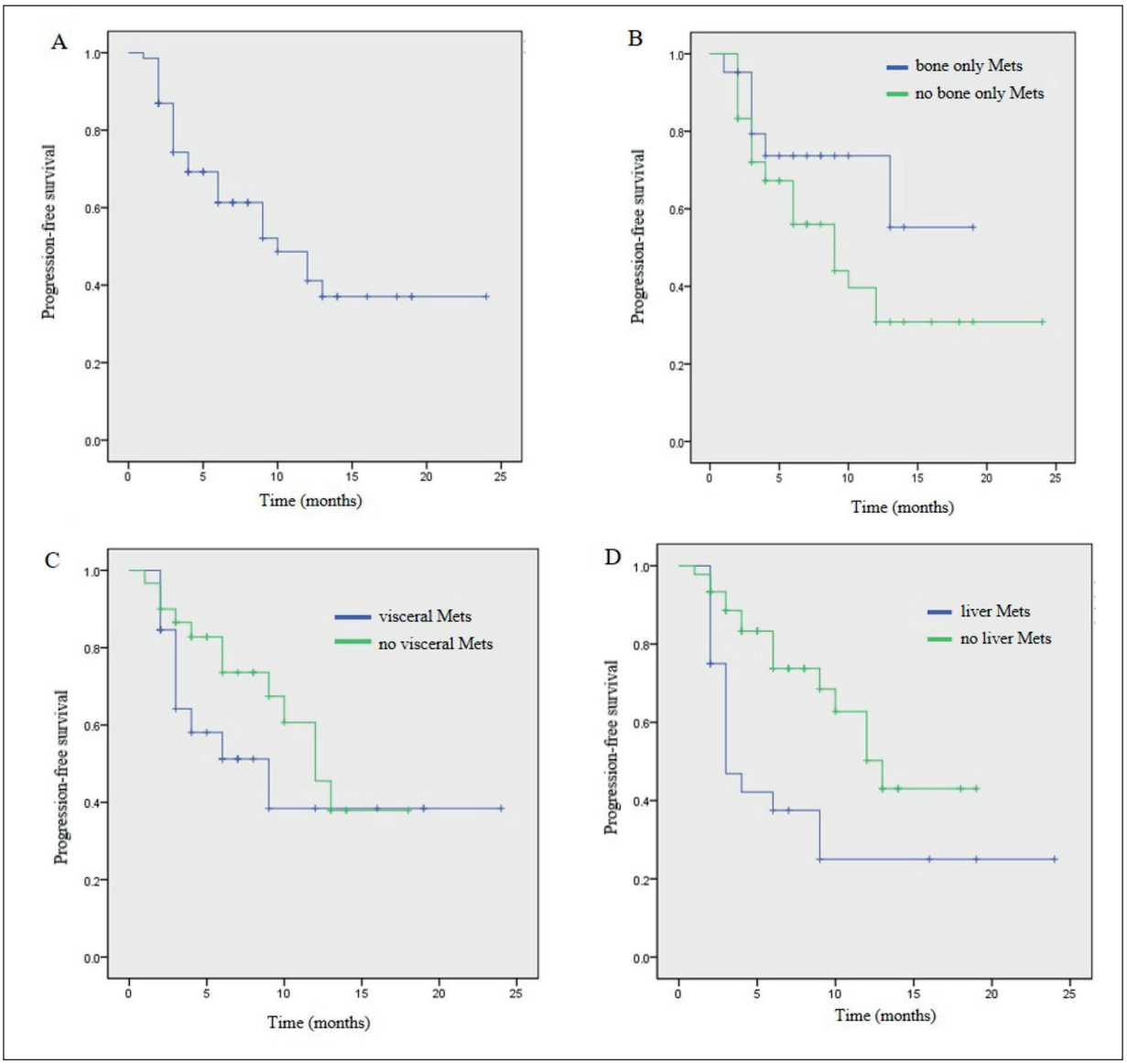

Figure 1. Kaplan-Meier curve for PFS in the overall population and according to the presence of bone metastasis, visceral involvement, and liver metastasis.

ble IV). The dose of palbociclib was reduced to 100 mg/day for 17 (24.6%) patients and 75 mg for only two (2.9%) patients (Table IV). In the IRIS study, patients were allowed to start at a lower dose (100 or 75 mg/day) of palbociclib. Therefore, the dose reduction rate was lower in the IRIS study than that in the real-world setting for Chinese patients. All patients tolerated the drug well after dose adjustment. Dose reduction did not affect the clinical activity of palbociclib compared with that in patients without dose reduction [10.2 months (95% CI: 6.2-14.1) *vs.* 13.3 months (95% CI: 10.2-16.3), respectively; p = 0.332; Figure 2D].

Discussion

With the discovery of CDK4/6 inhibitors, the standard of care for patients with HR+/HER2- ABC/MBC has transitioned from endocrine monotherapy to endocrine-targeted therapy[18,19]. Many real-world experiences have been published to share the results of clinical practice in Europe, North America, and Latin America[10,11,20]. To date, palbociclib is the only available CDK4/6 inhibitor in Mainland China. This retrospective study summarized the dose-patterns and clinical benefits of this drug in the real-world setting in China, aiming to provide real-world experience of clinical practice in China.

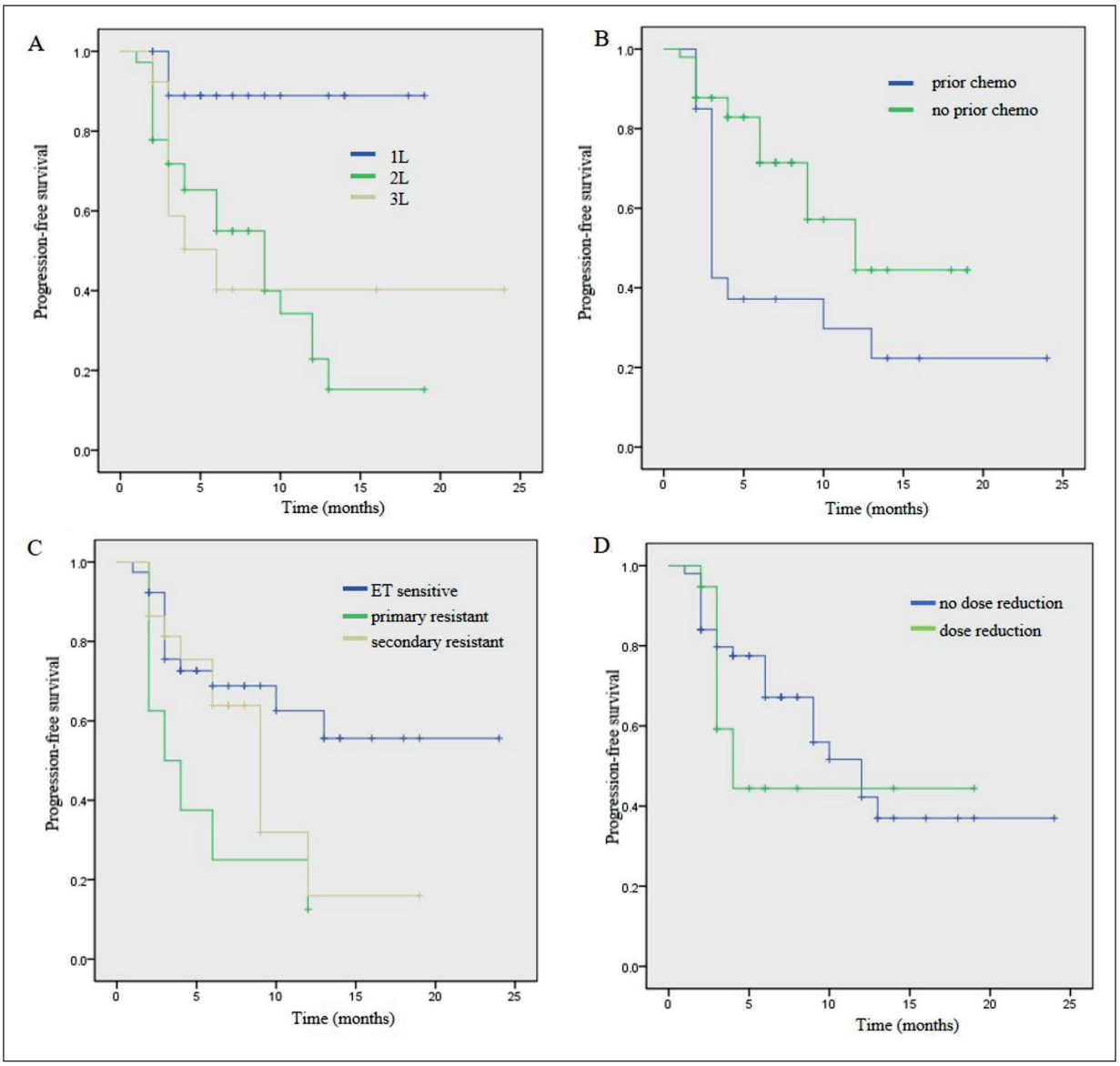

Figure 2. Kaplan-Meier curve for PFS according to lines of treatment, previous chemotherapy, previous ET, ET sensitivity, and dose reduction.

Table IV. Dose patterns of patients receiving palbociclib-based therapy.

		IRIS study (non-Chinese countriesl			
	China, n (%)	USA, n (%)	Argentina, n (%)	Canada, n (%)	Europe, n (%)
Starting Dose					
125 mg	69 (100)	492 (75.5)	140 (86.4)	221 (89.5)	920 (90.5)
100 mg	0	105 (16.1)	20 (12.3)	21 (8.5)	91 (8.9)
75 mg	0	55 (8.4)	2 (1)	5 (2.0)	6 (0.6)
Dose reduction					
Yes	19 (27.5)	113 (17.3)	20 (12.3)	37 (15.0)	145 (14.3)
No	50 (72.5)	539 (82.7)	142 (87.7)	210 (85.0)	872 (85.7)

In this study, the mean age of the Chinese patients was lower than that of the patients in the IRIS study. There were also more premenopausal patients among the Chinese BC patients because BC onset occurs at a younger age in China than in many other countries[21]. The mean age of Chinese patients at the time of diagnosis of BC is 44-45 years[22]. Moreover, such early onset BC is often more aggressive and associated with a poorer prognosis[23,24]. This may partially explain why the CBR and ORR were lower for Chinese patients in this study than those for the patients in the IRIS study. Patient race differed between our study and the IRIS study; however, no studies have demonstrated decreases in the efficacy of palbociclib.

The approval of palbociclib mainly depends on promising data from two large randomized clinical trials, PALOMA-2 and PALOMA-3[6,25]. In this retrospective analysis, the ORR and CBR were comparable to those in PALOMA-3, in which the ORR and CBR in the palbociclib plus fulvestrant arm were 19% and 67%, respectively[26]. The median PFS was 12.8 months in the overall population. This PFS was shorter than that in the PALOMA-2 study but comparable to that in the PALOMA-3 study[26,27]. The reason for this may be that half of the patients included in this real-world analysis were not treated with palbociclib as the first-line regimen. 21 (30.4%) patients had received palbociclib as the third or later line of treatment. As a result, the patients in this study were much more heavily pretreated with ET[25]. This may also explain why the CBR and ORR were lower for the Chinese patients than those for the patients in the IRIS study, because less than 10% of the patients were treated with palbociclib as the third or later line of treatment in the IRIS study. Therefore, sensitivity to palbociclib-ET treatment was reduced due to some unknown mechanism. Notably, the earlier palbociclib is prescribed, the more benefit will be obtained for patients with HR+/HER2- MBC. Furthermore, the assessment criteria for complete CR/PR were different; in this study, CR/PR was recorded at the first radiological assessment. In the IRIS study, CR/PR was recorded at any time during treatment (no 24-week minimum)[12]. Thus, there is no doubt that ORR and CBR were higher for the non-Chinese patients than those for the Chinese patients owing to differences in the assessment timing.

Bone metastases account for 60-80% of the MBC cases[28]. The prognosis of patients with bone-only metastatic BC was better than that of the patients with other types of MBC[29]. In the current study, patients with bone-only metastases had a longer PFS (15.4 months) than those without bone-only metastases (11.4 months), and this is consistent with the data (median PFS of bone-only disease: 14.3 months) for the combination of palbociclib and fulvestrant in the PALOMA-3 study[30]. However, only 12 (17.4%) patients had bone-only metastases, and this number was much lower than that of the patients from the USA and Europe in the IRIS study. Accordingly, BC encountered in this study was more aggressive than that in the IRIS study. The median PFS for patients with visceral metastasis was 11.9 months, which was similar to the median PFS observed in the results from the PALOMA-3 study (8.0 months)[26] but much shorter than that observed in the PALOMA-2 study (19.3 months)[27]. Interestingly, the median PFS for patients with liver metastases (8.9 months) was shorter than that observed in the PALOMA-2 study (13.7 months) but longer than that observed in the PALOMA-3 study (7.5 months)[30]. This difference indicated that Chinese patients with liver metastases may be more sensitive to treatment with palbociclib and ET. Patients with liver metastases could benefit from a stronger ET schedule, such as ET with palbociclib. However, there were only 69 patients included in the current study. Therefore, more real-world data are required to provide solid real-world evidence for the validation of these findings.

The prognosis of heavily pretreated patients with MBC is known to be very poor[20,31,32]. Therefore, the current study compared differences in patients with and without prior chemotherapy, prior lines of therapy, and sensitivity to ET. A shorter PFS was observed for patients who had received prior chemotherapy and/or ET. Moreover, patients who had received the first line of treatment showed a longer PFS than patients who had received two or more lines of treatment. These data suggested that earlier use of palbociclib-ET may be associated with more clinical benefits in patients with HR+/HER2- MBC. These data were also consistent with the data from the IRIS study[10-13], the MONARCH-2 and MONALEESA-3 trials[33,34], and real-world findings from other countries[10,35]. Furthermore, sensitivity to ET was also a prognostic indicator of the clinical efficacy of the combination of palbociclib and ET. Sensitivity to the combined treatment decreased in the following order: endocrine sensitive > primary resistant > secondary resistant. Interestingly, one patient received palbociclib and tamoxifen as the third line of treatment and had a PFS of more than

2 years. Until the date of data cut-off, this patient was still undergoing the treatment with palbociclib and tamoxifen and had not shown disease progression. More patient data should be collected to determine the factors contributing to patient sensitivity to palbociclib.

Palbociclib was well tolerated in this real-world study. Indeed, 27% of the patients underwent at least one dose reduction during the treatment. This ratio was lower than that reported in the PALOMA-2 (36%) and PALOMA-3 (34%) studies[6,26]. The main reason for dose reduction was hematological toxicity (neutropenia and leucopenia; data not shown). Dose reduction did not affect the clinical activity of palbociclib, and this is consistent with the data from PALOMA-2, PALOMA-3, and other real-world studies[36-38].

There were some limitations to this study. Firstly, only 69 patients with MBC were included in this study, and more real-world data should be collected to facilitate the clinical use of palbociclib in China. Additionally, most patients in this study were pretreated with ET/chemotherapy before prescribing palbociclib; thus, data for first-line treatment with palbociclib and ET were limited in this real-world setting. Finally, the data were obtained from only two centers; therefore, in future studies, researchers should use data from additional centers in various regions of China.

Conclusions

In conclusion, this retrospective study confirms that palbociclib combined with ET is effective for Chinese patients with MBC in a real-world setting. A longer PFS was observed for patients with bone-only metastases, no liver metastases, no previous palliative chemotherapy, no previous palliative ET, and ET sensitivity. To the best of our knowledge, this is the first study comparing palbociclib-based therapy in China with a multi-country, real-world study. This comparison could provide new insights into the potential outcomes of palbociclib-based therapy under different treatment settings. In addition, this comparison also showed the difference of BC onset ages, menopausal statuses, and prognosis between patients from China and from non-Chinese countries. When comparing real-world experience with the results of the IRIS study, it was found that patient age, menopausal status, and lines of treatment were different between the IRIS study and the Chinese real-world setting. These differences reflected demographic variations in breast cancer onset, such as age and menopausal status. With regard to lines of treatment, palbociclib was approved for use in China later than it was approved in North America, Argentina, and Europe; therefore, most patients had already received systemic treatment for MBC when palbociclib became available in China. The clinical outcomes of this study will provide real-world experience to physicians and facilitate the optimization of therapeutic regimens for patients with HR+/HER2- MBC.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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