Treatment patterns and clinical outcomes in patients with metastatic breast cancer treated with palbociclib-based therapies: real-world data in the Han population

Hongnan Mo, Fei Ma, Qing Li, Pin Zhang, Peng Yuan, Jiayu Wang, Yang Luo, Ruigang Cai, Qiao Li, Binghe Xu

Department of Medical Oncology, National Cancer Center, National Clinical Research Center for Cancer, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China.

Abstract

Background: This study aimed to reveal the treatment patterns and clinical outcomes of diverse palbociclib-based regimens in Han patients with estrogen receptor-positive (ER+) metastatic breast cancer in routine clinical practice.

Methods: The clinical data of patients with ER+ metastatic breast cancer treated with palbociclib were collected from the National Cancer Center database. The efficacy profile of palbociclib in this Han population was evaluated, especially for various combination regimens. The efficacy of palbociclib-based therapy in patients with prior everolimus treatment was also assessed.

Results: A total of 186 patients from 89 cities in 18 provinces in China were enrolled. The median progression-free survival (PFS) was similar among different palbociclib-combined groups ($P = 0.566$): 10.0 months (95% confidence interval [CI] 3.8–16.1) in the +exemestane group, 9.7 months (95% CI 6.3–13.1) in the +letrozole group, 7.8 months (95% CI 5.5–10.2) in the +fulvestrant group, 7.2 months (95% CI 3.2–11.3) in the +toremifene group, and 6.1 months (95% CI 1.2–11.0) in the +anastrozole group. Thirty-four patients (18.3%) had received everolimus for their metastatic disease before the prescription of palbociclib. The disease control rate was significantly lower in patients who had received previous everolimus than in the everolimus-naïve group (50.0% vs. 82.2%, $P < 0.001$). Patients pre-treated with everolimus had significantly worse PFS than those in the everolimus-naïve group (3.4 months vs. 8.8 months, $P = 0.001$). After propensity score matching, patients pre-treated with everolimus had similar PFS (4.4 months, 95% CI 0.5–8.2) compared with everolimus-naïve patients (6.1 months, 95% CI 4.7–7.5, $P = 0.439$).

Conclusions: Various palbociclib-based regimens have promising efficacy in ER+ metastatic breast cancer in real-world settings, even in patients who had been pre-treated with everolimus.

Keywords: Metastatic breast cancer; Palbociclib; Progression-free survival; Real-world data

Introduction

Breast cancer is the most diagnosed carcinoma among women in China and worldwide,[1,2] and estrogen receptor positive (ER+) breast cancer is the most common subtype.[3] In these patients, significant advantages for survival were observed for cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors, including palbociclib, ribociclib, and abemaciclib.[4-6] In the settings of clinical trials, palbociclib in combination with fulvestrant or letrozole as first-line treatment has significantly prolonged progression-free survival (PFS) in ER+ metastatic breast cancer patients from 6.6 months to 10.3 months with tolerable side effects.[7,8] However, patients in clinical trials cannot represent all patients in routine clinical settings, such as those with bone-only metastasis. The efficacy of palbociclib in these patients is not clear. Real-world data from the United States, mainly from White people, have supported the benefits of the addition of CDK4/6 inhibitors as first-line treatment for improving long-term outcomes.[9-11] Real-world data from other races may further support the value of CDK4/6 inhibitors in patients with ER+ metastatic breast cancer.

Recently, studies of the mechanisms of resistance to CDK4/6 inhibitors have focused on the phosphatidylinositol-3-kinase/Akt (PI3K/Akt) and mammalian target of rapamycin (mTOR) pathway. Abnormalities in this pathway occur in >40% of ER+ breast cancers and the most common one is PIK3CA gene mutation.[12] Activation of the PI3K/Akt/mTOR pathway is a critical step in oncogenesis and plays an important role in the

development of endocrine resistance for ER+ breast cancers.[13,14] Recently, upregulated PI3K/Akt/mTOR signal has been found in response to chronic exposure to CDK4/6 inhibitors which bypasses the CDK4/6 axis and subsequently drives cell cycle progression.[15] Because of this, the Palbociclib Ongoing Trials in the Management of Breast Cancer 3 (PALOMA-3) trial excluded patients who had previously received everolimus, an mTOR inhibitor. Consequently, the clinical outcomes of CDK4/6 inhibitor combinations in patients previously treated with mTOR inhibitors are poorly understood.

Here, we conducted a cohort study in patients with ER+ metastatic breast cancer using the National Cancer Center database. The efficacy profile of palbociclib (the only available CDK4/6 inhibitor in China) in the real-world setting in the Han population was investigated. Furthermore, the clinical outcomes of palbociclib-based treatment in patients with prior exposure to everolimus (mTOR inhibitor; PI3K/Akt inhibitors are not available in China at present) were compared to those of everolimus-naïve patients.

Methods

Study design and patient population

The medical charts of patients who were prescribed palbociclib from May 1, 2016 to November 30, 2019 were collected from the database of the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and reviewed. Patients were included if they (1) were diagnosed with metastatic breast carcinoma, (2) had confirmed ER+ human epidermal growth factor receptor 2-negative (HER2−) tumors, (3) received palbociclib-containing treatment, and (4) completed at least 1 month of follow-up after the prescription. The clinical and pathological characteristics of the patients were analyzed. The ER and Ki-67 status were evaluated based on metastatic biopsy results, except for those with bone-only metastasis, which were evaluated based on the primary lesion. The efficacy profile of palbociclib in this Han population was evaluated, especially in patients younger than 40 years, in those with bone-only metastasis, as different treatment lines, and for various combination regimens. The efficacy of palbociclib-based therapy in patients with prior everolimus treatment was also assessed.

Ethics

The study was authorized by the review board of the Cancer Hospital, Chinese Academy of Medical Sciences (19/331–2115), and all patients signed informed consent before treatment. The procedures were in accordance with the *Helsinki Declaration* and the Good Clinical Practice guidelines.

Statistical analysis

Patients' baseline characteristics were categorized and compared using χ^2 tests. The visceral disease was defined as metastatic breast cancer with visceral organ involvement (lung, liver, peritoneum, or pleura) that was present at the initiation of palbociclib treatment. A propensity

score for previously receiving everolimus was estimated using logistic regression with the following covariates: age, stage at diagnosis, progesterone receptor-positive rate, Ki-67 positive rate, and previous lines of treatment.

Primary resistance to endocrine therapy is defined as a relapse within 2 years of adjuvant endocrine treatment, or disease progression during the first 6 months of first-line endocrine therapy for metastatic breast cancer. Secondary resistance to endocrine therapy is defined as relapse while on adjuvant endocrine therapy but after the first 2 years of treatment, relapse within 12 months of completing adjuvant endocrine therapy, or progressive disease 6 months or more months after starting endocrine therapy for metastatic breast cancer.[16] The disease control rate (DCR) was defined as the percentage of patients who achieved complete response, partial response, or stable disease after treatment. PFS was defined as the time from the initiation of palbociclib to the date of disease progression which was determined by the physician based on available radiologic information, hematologic tumor markers, and/or clinical information. The Kaplan–Meier method and log-rank test were used to estimate and compare survival curves, both in the original population and in the matched population according to the propensity scores. Cox regression analysis was applied to identify independent predictors of survival in the multivariate analysis. A two-sided P value < 0.05 was considered statistically significant. All statistical analyses were carried out using IBM SPSS version 24.0 software (IBM Corp., Armonk, NY, USA), including propensity-score matching.

Results

Patient characteristics

From May 1, 2016, to November 30, 2019, a total of 186 patients were enrolled in this study [Figure 1]. Patients
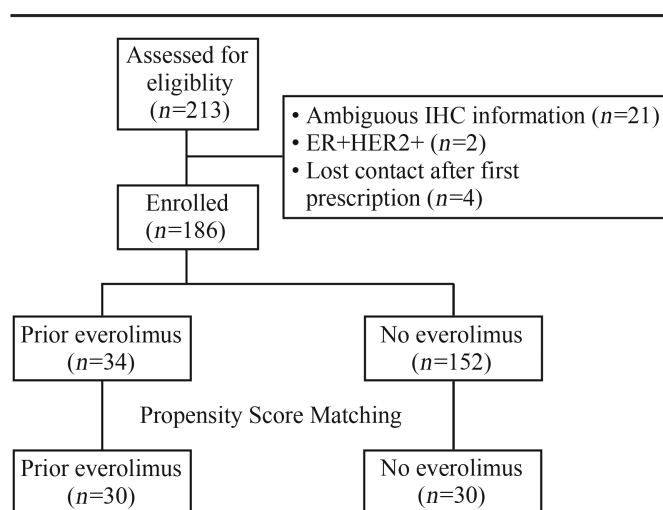

Figure 1: Patient flow diagram. The medical charts of 213 ER+ patients who had been prescribed palbociclib from May 1, 2016 to November 30, 2019 were reviewed. A total of 27 patients were excluded because of ambiguous IHC information (N = 21), HER2-positive disease (N = 2), and lost follow-up (N = 4). Of the enrolled 186 patients, 34 patients had received everolimus before the prescription of palbociclib. Propensity score matching was used to match patients with or without prior everolimus treatment and resulted in 30 patients in the previous-everolimus group and 30 patients in the everolimus-naïve group. ER+: Estrogen receptor-positive; HER2+: Human epidermal growth factor receptor 2-positive; IHC: Immunohistochemistry.

were from 89 cities in 18 provinces in China. The greatest number of patients come from five regions: Beijing (74, 42.5%), Hebei (28, 15.1%), Shandong (15, 8.1%), Inner Mongolia (13, 7.0%), and Heilongjiang (11, 5.9%). The median age was 54 years (range 28–90), and 29 patients (15.6%) were younger than 40 years. Thirty-three patients (17.7%) had *de novo* metastatic breast cancer. One hundred and thirty-eight (74.2%) patients had visceral disease when they started the palbociclib therapy, while 16 (8.6%) patients had bone-only metastasis. Among these 186 patients, 42 patients were primarily resistant to all endocrine drugs they had used, and 80 patients had developed a secondary resistance to at least one endocrine drug. Patients received distinct endocrine therapy combined with palbociclib: 96 with fulvestrant, 45 with letrozole, 20 with exemestane, 14 with anastrozole, nine

with toremifene, and two with medroxyprogesterone. Only 48 patients (25.8%) received palbociclib as first-line treatment for their metastatic disease, while 82 patients (44.1%) had previously undergone at least three lines of systemic treatment. Thirty-four patients (18.3%) had received everolimus for their metastatic disease before the prescription of palbociclib. The basic clinical and pathological characteristics are detailed in Table 1. As of February 2020, the median follow-up time was 6.5 months (range 0.9–40.0), and 88 patients had disease progression.

Efficacy profile of palbociclib in the Han population

The DCR after palbociclib-based treatment was promising in patients with bone-only metastasis (93.7% *vs.* 74.7%,

Table 1: Clinical and pathological characteristics before and after matching on the propensity score n (%).

Characteristics	All (n = 186)	Before matching			After matching		
		Previous mTORi (n = 34)	mTORi-naïve (n = 152)	P values	Previous mTORi (n = 30)	mTORi-naïve (n = 30)	P values
Age				0.260			0.354
<40 years	29 (15.6)	4 (11.8)	25 (16.4)		3 (10.0)	3 (10.0)	
40–69 years	140 (75.3)	29 (85.3)	111 (73.0)		27 (90.0)	25 (83.3)	
≥70 years	17 (9.1)	1 (2.9)	16 (10.6)		0	2 (6.7)	
Stage at diagnosis				0.328			1.000
I–III	153 (82.3)	26 (76.5)	127 (83.6)		24 (80.0)	24 (80.0)	
IV	33 (17.7)	8 (23.5)	25 (16.4)		6 (20.0)	6 (20.0)	
*ER+				0.003			1.000
1–9%	4 (2.2)	3 (8.8)	1 (0.7)		1 (3.3)	1 (3.3)	
≥10%	182 (97.8)	31 (91.2)	151 (99.3)		29 (96.7)	29 (96.7)	
*PR+				0.283			0.292
1–9%	62 (33.3)	14 (41.2)	48 (31.6)		14 (46.7)	10 (33.3)	
≥10%	124 (66.7)	20 (58.8)	104 (68.4)		16 (53.3)	20 (66.7)	
*Ki-67+				0.426			0.488
0–13%	25 (13.4)	6 (17.6)	19 (12.5)		6 (20.0)	4 (13.3)	
≥14%	161 (86.6)	28 (82.4)	133 (87.5)		24 (80)	26 (86.7)	
Visceral disease				0.229			0.718
Yes	138 (74.2)	28 (82.4)	110 (72.4)		25 (83.3)	26 (86.7)	
No	48 (25.8)	6 (17.6)	42 (27.6)		5 (16.7)	4 (13.3)	
Bone-only disease				0.193			1.000
Yes	16 (8.6)	1 (2.9)	15 (9.9)		1 (3.3)	1 (3.3)	
No	170 (91.4)	33 (97.1)	137 (90.1)		29 (96.7)	29 (96.7)	
Number of metastatic sites				0.530			0.338
1–2	114 (61.3)	18 (52.9)	96 (63.2)		17 (56.7)	17 (56.7)	
3–4	64 (34.4)	14 (41.2)	50 (32.9)		13 (43.3)	11 (36.7)	
5–6	8 (4.3)	2 (5.9)	6 (3.9)		0	2 (6.6)	
Previous lines of therapy				<0.001			0.692
0	48 (25.8)	0	48 (31.6)		0	1 (3.3)	
1–2	56 (30.1)	6 (17.6)	50 (32.9)		6 (20.0)	4 (13.3)	
3–4	44 (23.7)	8 (23.5)	36 (23.7)		8 (26.7)	9 (30.0)	
≥5	38 (20.4)	20 (58.8)	18 (11.8)		16 (53.3)	16 (53.3)	
Endocrine sensitivity				0.409			0.683
Primary resistant	42 (22.6)	7 (20.6)	35 (23.0)		6 (20.0)	6 (20.0)	
Secondary resistant	80 (43.0)	18 (52.9)	62 (40.8)		15 (50.0)	12 (40.0)	
Sensitive	64 (34.4)	9 (26.5)	55 (36.2)		9 (30.0)	12 (40.0)	

*ER, PR, and Ki-67 status was evaluated based on metastatic biopsy results, except for those with bone-only metastases, which were evaluated based on the primary lesion. ER+: Estrogen receptor-positive; mTORi: Mammalian target of rapamycin inhibitor; PR: Progesterone receptor.
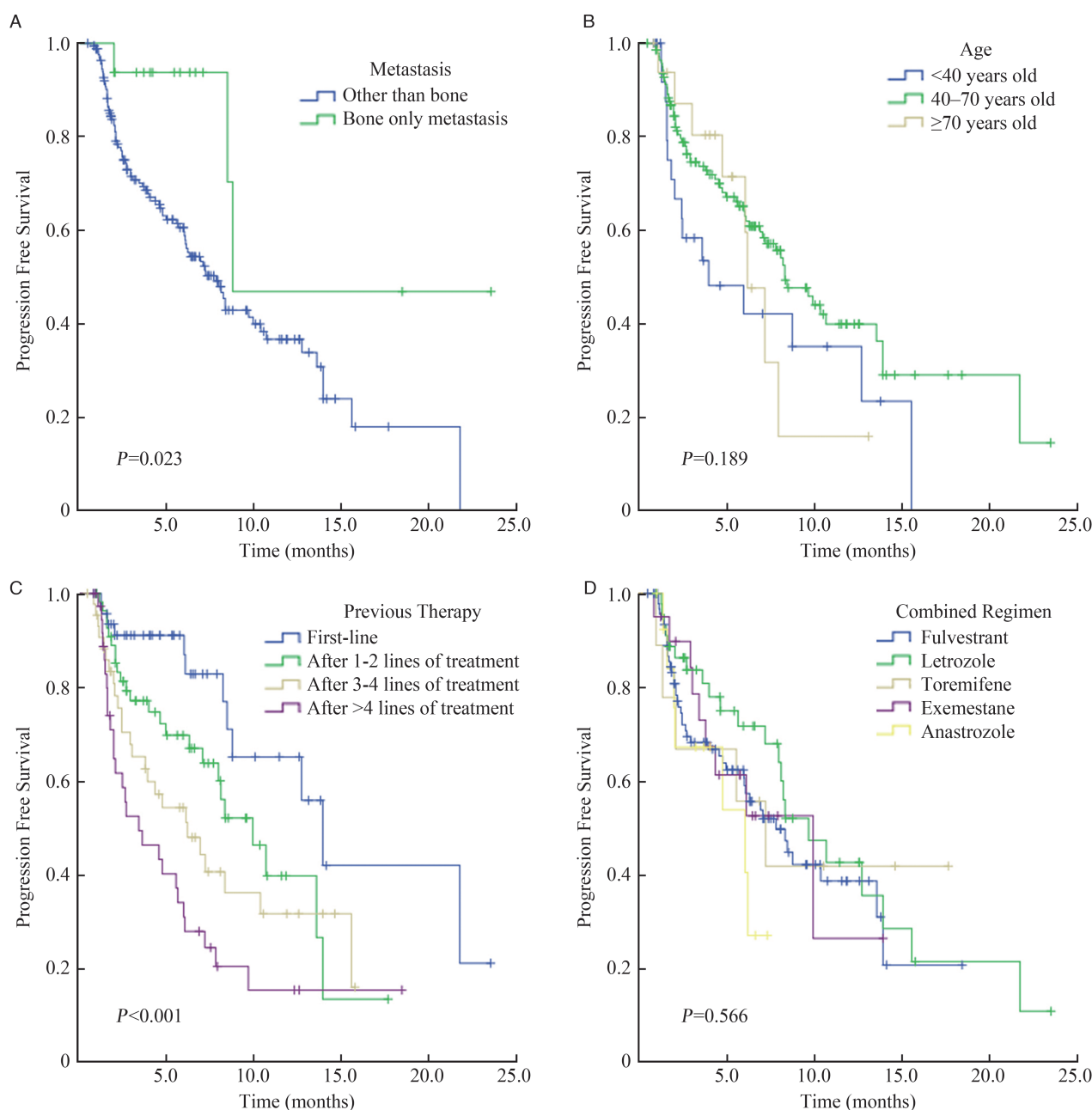
Figure 2: Kaplan–Meier curves revealing PFS according to the metastatic site (A), age (B), previous lines of treatment (C), and various regimen combinations (D). Patients with bone-only metastasis had significantly prolonged PFS compared with the other patients ($P = 0.023$; Figure 2A). The efficacy of palbociclib-based treatment decreased significantly in accordance with increasing numbers of previous lines of systemic treatment ($P < 0.001$; Figure 2C). Meanwhile, the median PFS was similar among different age groups and palbociclib-combined groups (both $P > 0.1$, Figure 2B,D). PFS: Progression-free survival.

$P = 0.087$), and these patients also had significantly prolonged PFS compared with the other patients (8.8 months *vs.* 7.8 months, $P = 0.023$; Figure 2A). The DCR of palbociclib-based therapy varied significantly among different age groups ($P = 0.034$), that is, the DCR was 60.0% (20/29) in patients younger than 40 years, 77.1% (108/140) in those aged 40 to 70 years, and 82.3% (14/17) in patients older than 70 years. Meanwhile, patients younger than 40 years had a similar PFS (4.0 months, 95% confidence interval [CI] 0–8.5) when compared with patients older than 40 years (8.4 months

in those aged 40–70 years, and 6.2 months in those older than 70 years, $P = 0.189$; Figure 2B).

The efficacy of palbociclib-based treatment changed in accordance with increasing numbers of previous lines of systemic treatment [Figure 2C]. As the number of previous lines of systemic treatment increased, the DCR gradually decreased ($P = 0.001$), that is, the DCR was 93.7% (45/48) in the setting of first-line treatment, 80.3% (45/56) in patients with one to two prior regimens, 65.9% (29/44) in patients with three to four prior regimens, and 60.5% (23/

38) in patients who had been treated with more than five regimens. The median PFS was also longer in patients who had received palbociclib-based therapy as first-line treatment (14.0 months, 95% CI 11.4–16.6) than in those who received subsequent lines of treatment ($P < 0.001$), that is, 10.0 months (95% CI 7.1–12.9) in the second/third-line group, 6.2 months (95% CI 3.0–9.5) in the fourth/fifth-line group, and 3.4 months (95% CI 0.8–6.1) in patients who had received more than five lines of systemic therapy.

The DCR did not differ significantly among patients who received diverse palbociclib-based treatment ($P = 0.403$), that is, the DCR was 86.7% (39/45) in the letrozole-combined group, 74.0% (71/96) in the fulvestrant-combined group, 71.4% (10/14) in the anastrozole-combined group, 70.0% (14/20) in the exemestane-combined group, and 66.7% in the toremifene-combined group (6/9). The median PFS was also similar among different palbociclib-combined groups ($P = 0.566$; Figure 2D), that is, 10.0 months (95% CI 3.8–16.1) in the exemestane plus palbociclib group, 9.7 months (95% CI 6.3–13.1) in the letrozole plus palbociclib group, 7.8 months (95% CI 5.5–10.2) in the fulvestrant plus palbociclib group, 7.2 months (95% CI 3.2–11.3) in the toremifene plus palbociclib group, and 6.1 months (95% CI 1.2–11.0) in the anastrozole plus palbociclib group. One of the two patients receiving medroxyprogesterone plus palbociclib had stable disease for >12 months; however, palbociclib treatment was interrupted for financial reasons. The other patient experienced disease progression after 2.5 months of treatment with medroxyprogesterone plus palbociclib.

Univariate analysis revealed that patients who were younger than 40 years ($P = 0.022$), those with metastasis other than bone metastasis ($P = 0.069$), and those who had received previous lines of systemic treatment ($P < 0.001$) seemed to have worse PFS, while various treatment combinations ($P = 0.763$), number of metastatic sites ($P = 0.508$), and disease stage at diagnosis ($P = 0.620$) did not influence PFS. Multivariate analysis [Table 2] showed that age and previous lines of systemic

treatment before palbociclib-based therapy were both independent factors for PFS ($P = 0.027$ and $P < 0.001$, respectively).

Efficacy in patients with prior everolimus treatment

The median time between the end of the previous everolimus and the start of palbociclib was 7.9 months (range 0–35.8; Supplementary Figure 1, http://links.lww.com/CM9/B139). Three patients (8.8%) discontinued everolimus therapy because of mucositis and pneumonitis. Regarding the prior everolimus regimens, everolimus was mostly combined with aromatase inhibitors (21/34, 61.8%), followed by fulvestrant (7/34, 20.6%), and toremifene (6/34, 17.6%). Aromatase inhibitors plus everolimus exhibited similar DCR (16/21, 76.2%, $P = 0.205$) compared with other everolimus combinations: 42.9% (3/7) in patients received everolimus plus fulvestrant, and 50.0% (3/6) in those received everolimus plus toremifene. The median PFS of everolimus-containing treatment in these 34 patients was 5.2 months (95% CI 2.6–7.8), which was not significantly different among the various combinations ($P = 0.057$; Supplementary Figure 2A, http://links.lww.com/CM9/B139). Whether the disease was controlled or not after the previous everolimus treatment was not significantly correlated with the DCR of the subsequent palbociclib regimen ($P = 0.297$; Supplementary Figure 2B, http://links.lww.com/CM9/B139).

The DCR was significantly lower in patients who had received previous everolimus (50.0%, 17/34) than in the everolimus-naïve group (82.2%, 125/152, $P < 0.001$). Consistently, the Kaplan–Meier estimates indicated that patients pre-treated with everolimus had significantly worse PFS (3.4 months, 0.7–6.1) than patients in the everolimus-naïve group (8.8 months, 95% CI 6.6–11.0, $P = 0.001$; Figure 3A). Further, propensity score matching was used to match patients with or without prior everolimus treatment. Propensity score matching resulted in 30 patients in the previous-everolimus group and 30 patients in the everolimus-naïve group [Table 1]. After propensity score matching, no significant differences in the clinical characteristics were observed between the two groups. Palbociclib-based therapy seemed to result in a slightly worse DCR of 53.3% (16/30) in the previous-everolimus group compared with 76.7% (23/30) in the everolimus-naïve group ($P = 0.058$). Patients pre-treated with everolimus had similar PFS (4.4 months, 95% CI 0.5–8.2) when compared with everolimus-naïve patients (6.1 months, 95% CI 4.7–7.5, $P = 0.439$; Figure 3B).

Discussion

Our study showed the real-world efficacy of palbociclib-based treatment in the Han population, based on data from patients in multiple cities in China. It is worth noting that some of these patients have bone-only metastasis, and were not suitable for clinical trials due to the lack of measurable target lesions. In addition, the endocrine therapy drugs used in combination with palbociclib are not limited to fulvestrant or letrozole that have been

Table 2: Multivariate analysis of PFS in patients treated with palbociclib-based therapy.

Variable	HR (95% CI)	P value
Age		0.038
<40 years	1.0	
40–70 years	0.50 (0.28–0.87)	0.014
≥70 years	0.76 (0.32–1.79)	0.526
Previous lines of treatment		<0.001
0	1.0	
1–2	2.03 (0.97–4.23)	0.060
3–4	2.77 (1.33–5.72)	0.006
≥5	5.10 (2.48–10.50)	<0.001
*Bone-only metastasis	0.36 (0.11–1.18)	0.091

* The control group included patients without bone metastases, as well as patients with metastases in other locations, including distant lymph node metastasis and visceral metastasis. CI: Confidence interval; HR: Hazard ratio; PFS: Progression-free survival.
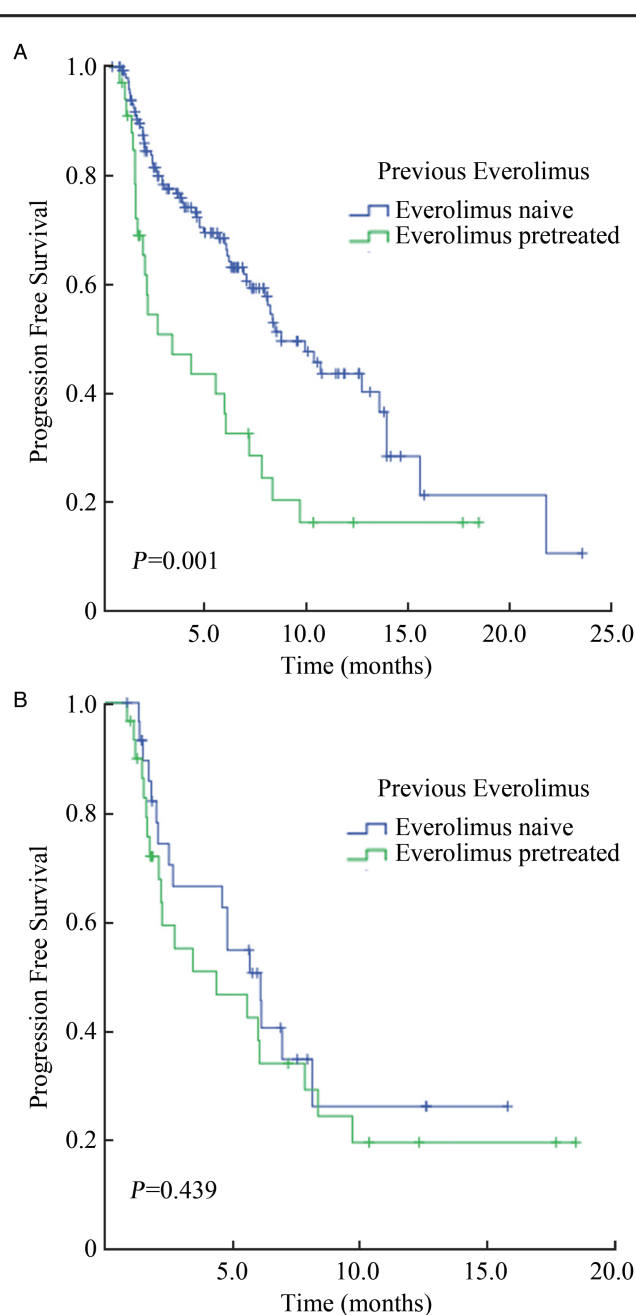
Figure 3: Kaplan–Meier estimates of PFS for various everolimus combinations in patients with metastatic breast cancer. (A) Patients pre-treated with everolimus had significantly worse PFS (3.4 months, 0.7–6.1) than those in the everolimus-naïve group (*P* = 0.001). (B) After propensity score matching, no significant differences in the clinical characteristics were observed between the two groups (*P* = 0.439). PFS: Progression-free survival.

verified in clinical trials. Therefore, the real-world efficacy data of these patients can be used as a good supplement to clinical trial data.

Palbociclib-based therapy as first-line systemic treatment resulted in a median PFS of 14.0 months in our patients. The efficacy profile of palbociclib-based treatment in this Han population was similar to the real-world clinical outcomes in patients from the United States.[9,11,17] These results seem to be worse when compared to the PFS data from the PALOMA-2 study (palbociclib plus letrozole,

median PFS 24.8 months), but a little bit better than that in the PALOMA-3 study (palbociclib plus fulvestrant, median PFS 9.5 months).[7,8,18] It is worth noting that the PALOMA-2 study excluded patients with acquired resistance to endocrine therapy (prior adjuvant endocrine treatment with DFI ≤ 12-months from completion of treatment, NCT01740427), but the PALOMA-3 study included these patients (progressed within 12 months from prior adjuvant endocrine therapy, NCT 01942135). The main explanation for the unusual lower PFS in our study might be that more than half of the patients enrolled in this study were already endocrine-resistant patients, even though endocrine drugs might have been effective before.

Significant differences between real-world patients and those in clinical trials should be considered. We included patients with bone-only metastasis who lacked measurable lesions. These patients are not uncommon in clinical settings; however, they are usually ineligible for clinical trials because of a lack of target lesions. In the bone-only metastasis subgroup of our patients, palbociclib-based combinations showed promising efficacy. Similarly in the PALOMA-2 study, it was also found that the benefit of the combination of palbociclib in the bone-only metastases subgroup (hazard ratio [HR] = 0.41) appeared to be more significant than that in the overall population (HR = 0.563).[7] One possible explanation may be that the survival prognosis of patients with bone-only metastasis is better than that of others since they have no visceral organ involvement.[19]

Notably, we found that the clinical efficacy of the various palbociclib-based regimens was similar, including exemestane plus palbociclib, and toremifene plus palbociclib regimens. Thus, endocrine therapy in combination with palbociclib may not be limited to fulvestrant and letrozole. Exemestane or toremifene in combination with palbociclib may be considered as an option in clinical trials for patients who are resistant to fulvestrant and letrozole after previous systemic treatment. Several clinical trials have been launched to evaluate the efficacy of exemestane plus palbociclib in patients with metastatic breast cancer (NCT02871791, NCT02592746).

Moreover, we enrolled patients who had undergone intensive treatment with more than five lines of systemic treatment; these patients had a terrible median PFS of 3.4 months after palbociclib-based combinations. These patients comprise a considerable proportion of the patient population in clinical practice; however, they are usually underrepresented in clinical trials. Since CDK4/6 inhibitors are not covered by medical insurance in China, a substantial proportion of patients cannot afford these drugs. Therefore, it is recommended that clinicians consider the economic benefit ratio in the future and take care to avoid using palbociclib-based regimens in these heavily pre-treated patients.

Several preclinical studies have shown that the activation of the PI3K/Akt/mTOR pathway may result in resistance to CDK4/6 inhibitors.[1,5,20,21] Thus, the PALOMA-3 trial excluded patients who had previously received

everolimus, an mTOR inhibitor. Meanwhile, a prospective single-arm clinical trial in France that evaluated the efficacy of palbociclib plus fulvestrant reported a DCR of 71.7% and median PFS of 5.8 months in patients pre-treated with everolimus.[22] In this study, we also analyzed the efficacy of palbociclib in patients with or without previous everolimus treatment. In the whole population, we found that patients who had been treated with everolimus had significantly worse DCR (50.0%) and PFS (3.4 months) than everolimus-naïve patients (DCR 82.2%, PFS 8.8 months). This finding appears to be consistent with that of a retrospective study of 23 patients in the United States.[23] In that study, Dhakal et al[23] found that palbociclib-based therapy had a DCR of 17.4% and a median PFS of 2.9 months in patients with metastatic breast cancer pre-treated with everolimus. Further, we used propensity score matching to reduce the interference of other variables such as previous lines of treatment. Subsequently, the difference between the patients with or without prior everolimus became less significant. Therefore, we believe that patients who have previously received everolimus treatment still have the opportunity to use palbociclib, and its efficacy is not worse than that of everolimus-naïve patients.

The limitations of our study should be considered. Our data originated from the retrospective review of medical charts in a single institution. However, the database of the China National Cancer Center covers most of the provinces in China which might reduce potential bias to some extent. This study included patients who received palbociclib between 2016 and 2019. The drug was officially approved for marketing in the mainland of China in 2018 and has not been covered by medical insurance by now. Therefore, the number of participants included in this study is limited. Only patients who could afford the drug received palbociclib, which may be a potential source of bias. Moreover, the evaluation of the clinical response did not involve independent radiological confirmation. Thus, our results should be interpreted with caution.

Conclusions

This real-world analysis revealed the treatment patterns and clinical outcomes after palbociclib-based combinations for ER+ metastatic breast cancer in the Han population. Our results demonstrated the promising efficacy of various regimens combined with palbociclib in real-world settings, even in patients with bone-only metastasis. Exemestane or toremifene could also be considered in combination with palbociclib in patients who are resistant to fulvestrant and letrozole after previous systemic treatment. Palbociclib may still be considered in patients who have previously received everolimus. Further studies with larger sample sizes and longer follow-ups are warranted to confirm our findings.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the review board of the Cancer Hospital, Chinese Academy of Medical Sciences (19/331–2115). Informed consent was obtained from all individual participants included in the study.

Consent to publish

The manuscript has been read and approved by all the authors. The requirements for authorship as stated earlier in this document have been met. Each author believes that the manuscript represents honest work, if that information is not provided in another form.

Conflicts of interest

None.

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