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Treatment patterns and clinical outcomes among patients receiving palbociclib in combination with an aromatase inhibitor or fulvestrant for HR+/HER2-negative advanced/metastatic breast cancer in real-world settings in the US: Results from the IRIS study

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ABSTRACT

Purpose: Palbociclib is a selective cyclin-dependent kinase (CDK) 4/6 inhibitor approved for use in postmenopausal women with hormone receptor-positive, human epidermal growth factor 2-negative (HR+/HER2-) advanced/metastatic breast cancer (ABC/MBC). Palbociclib has proven benefits in phase III placebo-controlled studies; however, real-world outcome data are lacking. The Ibrance Real World Insights (IRIS) study evaluated palbociclib use in patients with HR+/HER2- ABC/MBC in the real-world setting in the US, Argentina, and Germany. Here we describe results for the US patient subgroup.

Patients and methods: IRIS was a retrospective medical chart review study of patients with confirmed HR+/HER2- ABC/MBC who received palbociclib with either an aromatase inhibitor (AI) as initial endocrine-based therapy in postmenopausal women or fulvestrant-based therapy in women with disease progression following endocrine therapy. Physicians extracted data from patient medical records for ≤16 sequential patients each. Outcomes included progression-free and survival rates.

Results: Records were extracted for 652 patients: 360 (55.2%) treated with palbociclib + AI and 292 (44.8%) treated with palbociclib + fulvestrant. The 12-month progression-free rate was 84.1% for patients treated with palbociclib + AI and 79.8% for those treated with palbociclib + fulvestrant; 12-month survival rates were 95.1% for palbociclib + AI and 87.9% for palbociclib + fulvestrant.

Conclusion: In this first real-world assessment of clinical outcomes in US patients with HR+/HER- ABC/MBC, treatment with palbociclib in combination with AI or fulvestrant demonstrated favorable effectiveness in terms of progression-free and survival rates. Ongoing studies are needed to deliver mature clinical outcome data beyond 12/24 months in the real-world setting.

1. Introduction

Hormone receptor (HR)-positive, human epidermal growth factor 2 (HER2)-negative (HR+/HER2-) breast cancer is the most common breast cancer subtype in the US [1]. Although women with early-stage breast cancer generally have a good prognosis, women with distant metastases have a 5-year relative survival rate of just 27% [2].

For over a decade, hormonal therapies were the preferred initial treatment for patients with locally advanced or metastatic (ABC/MBC) HR+/HER2-breast cancers [3]; however, the success of these treatments is limited by high rates of de novo or acquired resistance [4]. Consequently, efforts have been made to identify new approaches incorporating other targeted treatments to overcome endocrine resistance.

Palbociclib is a selective cyclin-dependent kinase (CDK) 4/6 inhibitor approved for use in postmenopausal women with HR+/HER2- ABC/MBC in combination with an aromatase inhibitor (AI) as initial endocrine-based therapy, or with fulvestrant in women with disease progression following endocrine therapy [5]. The benefit for

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palbociclib in this population was confirmed in the phase III placebo-controlled PALOMA-2 study [6,7], in which patients treated with palbociclib + letrozole had a median PFS of 27.6 months versus 14.5 months for placebo + letrozole (hazard ratio = 0.58; p < 0.0001) [7]. In PALOMA-3, patients with relapsed/refractory HR+/HER2- ABC/MBC received palbociclib + fulvestrant or placebo + fulvestrant [8,9]; median PFS was superior with palbociclib + fulvestrant (9.5 vs 4.6 months, respectively; hazard ratio = 0.46; p < 0.0001) [9].

Treatment patterns and clinical effectiveness of palbociclib in patients with ABC/MBC have not been assessed extensively in the real-world setting. The multi-country Ibrance Real World Insights (IRIS) study is a retrospective chart review of women treated with palbociclib-based regimens according to approved indications in real-world clinical practice, aiming to describe their demographic and clinical characteristics, treatment patterns, and to assess clinical outcomes. Here we describe the results from patients in the US who were part of the IRIS study.

2. Patients and methods

2.1. Study design

IRIS was a retrospective medical chart review of patients who received palbociclib with either an AI or fulvestrant based on labeled indications [5]. In addition to the US, patients were recruited in Argentina and Germany; results from those countries will be reported separately. The study was conducted in accordance with International Society for Pharmacoepidemiology recommendations and Guidelines for Good Pharmacoepidemiology Practices. The study protocol and statistical analysis plan were approved by the Western Institutional Review Board.

2.2. Study population

Eligible physicians (oncologists, oncologist hematologists, or gynecologists) had to have prescribed palbociclib to at least 5 patients with HR+/HER2- ABC/MBC in line with the labeled indication in the US prescribing information [5]. Physicians were required to have first prescribed palbociclib + AI ≥180 days before or palbociclib + fulvestrant ≥90 days before the date of their enrollment to ensure they had patients with sufficient follow-up. Physicians were recruited from community and academic practices across the US using a soft quota maximum of 35% treating physicians from each region to ensure a geographic spread.

Eligible patients were required to be aged ≥18 years with a confirmed diagnosis of HR+/HER2- ABC/MBC. All patients had received palbociclib treatment as per the licensed indication(s) in the US, i.e. in combination with an AI as initial endocrine-based therapy in postmenopausal women (approved February 1, 2015) or in combination with fulvestrant in women with disease progression following endocrine therapy (approved February 19, 2016) [5]. A quota was implemented to ensure that ≥30% of selected patients had been treated with palbociclib + fulvestrant. No prior or current enrollment in interventional clinical trials for ABC/MBC was allowed. To ensure sufficient follow-up, patients must have initiated palbociclib + AI ≥180 days or palbociclib + fulvestrant ≥90 days before data collection. Patients were not required to be receiving palbociclib therapy for any minimum period of time.

2.3. Data source and extraction

Physicians extracted data from patient medical records to complete an electronic case report form. The index date was defined as 60 days after the physician first prescribed palbociclib + AI or fulvestrant following regulatory approval for specific indications in the US (e.g. if palbociclib + letrozole was approved in the US on February 1, 2015, and the physician initiated the patient on palbociclib + letrozole the next day, the index date was defined as April 2, 2015). The index dates therefore differed for the two indications as they were approved at different times. Starting with the index date, each physician selected up to 16 sequential medical records of patients who met the inclusion criteria. Data were extracted from the index date until the earliest of: last available medical record, death, or date of record abstraction.

Data extracted from patient medical records to complete the web-based study case report form included patient and clinical characteristics, e.g. age, ethnicity/race, menopausal status, Eastern Cooperative Oncology Group (ECOG) performance status (PS), and site(s) of metastases at MBC diagnosis. Palbociclib treatment patterns captured included starting dose, modifications, and reasons for palbociclib regimen changes and discontinuation. Best overall response and time to response, discontinuation, or death were also captured. Clinical outcomes derived from data collected included objective response rate (ORR), clinical benefit rate (CBR), and progression-free and survival rates at 6, 12, 18, and 24 months. Because of the implemented follow-up period, 18- and 24-month progression-free and survival rate data for fulvestrant were immature at the time of analysis. Response captured in the study reflected best response seen over time while on palbociclib combination therapy. Definitions of all clinical outcome variables are presented in Table 1.

2.4. Statistical analysis

Descriptive analyses were performed; no formal hypothesis was tested. Descriptive statistics were dependent on the variable described: continuous variables included respondent base, mean, median, standard deviation (SD), and range; categorical variables included number and percentage of responses in each category. Time to event outcomes at 6, 12, 18, and 24 months were calculated using Kaplan-Meier estimates. CBR data were censored for patients still receiving palbociclib but with <24 weeks' data available and no evidence of complete response (CR), partial response (PR), or progression. Patients with missing values for an endpoint were not included in the analysis of that endpoint; missing data were not imputed.

Analyses were conducted using STATA statistical software version 15.1 (StataCorp LLC, College Station, TX, USA).

3. Results

3.1. Physicians and patients

Between June and October 2017, 65 physicians (39 medical or clinical oncologists; 26 hematologists) extracted data; 41 (63.1%) were community oncologists, 21 (32.3%) were from academic centers, and 3 (4.6%) were from outpatient clinics. Thirty-three physicians (50.8%) had a caseload of 11–20 palbociclib-treated patients; 21 (32.3%) had >20 palbociclib-treated patients. The mean (SD) time since first prescribing palbociclib + AI was 23.5 (6.5) months and the mean time since first prescribing palbociclib + fulvestrant was 14.1 (3.4) months.

Records were extracted for 652 patients, 360 (55.2%) treated with palbociclib + AI and 292 (44.8%) with palbociclib + fulvestrant (Table 2). A total of 285 patients (43.7%) were diagnosed with ABC/MBC at initial diagnosis, comprising 233 (64.7%) in the palbociclib + AI group and 52 (17.8%) in the palbociclib + fulvestrant group. Overall, 89.4% of palbociclib + AI patients and 84.9% of

Table 1
Clinical outcomes and response definitions.

Response	Definition/variables
Clinical outcomes	
Complete response	Where 'Complete response' has been recorded at any time on treatment (no 24-week minimum)
Partial response	Where 'Partial response' has been recorded at any time on treatment (no 24-week minimum)
Stable disease ≥24 weeks	Patients remained on palbociclib for a minimum of 24 weeks without complete or partial response, death, treatment switch, or progression
Stable disease <24 weeks	Stable disease recorded for initial response, with a subsequent progression recorded after <24 weeks or treatment switch for reason other than progression after <24 weeks, or death without recorded progression after <24 weeks
Progressive disease	Progressive disease recorded for initial response without a subsequent partial or complete response recorded
Best response definitions	
Objective response rate	Proportion of patients achieving a complete or partial response as assessed by the physician and reported in the patient records; radiologic confirmation was not required and no criteria to re-evaluate was provided.
Clinical benefit rate	Proportion of patients who achieved a complete or partial response or had stable disease for ≥24 weeks as assessed by the physician
Progression-free rate	Proportion of patients with no evidence of progression or death at 6, 12, 18, and 24 months
Survival rate	Proportion of patients alive at 6, 12, 18, and 24 months
Time to progression	Time from start of palbociclib treatment to date of progression, death, or time of electronic case report form completion if the patient had not progressed or died

Table 2
Patient demographic and clinical characteristics.

Characteristic	Overall (n = 652)	Palbociclib + AI (n = 360)	Palbociclib + fulvestrant (n = 292)
Age at palbociclib initiation, years			
Mean (SD)	64.0 (10.9)	64.8 (10.4)	63.0 (11.4)
Median (range)	65.0 (30.0–90.0)	66.0 (32.0–90.0)	63.5 (30.0–90.0)
Ethnic origin, n (%)			
White/Caucasian	391 (60.0)	221 (61.4)	170 (58.2)
African American	119 (18.3)	70 (19.4)	49 (16.8)
Asian	24 (3.7)	9 (2.5)	15 (5.1)
Hispanic/Latino	71 (10.9)	40 (11.1)	31 (10.6)
Other	47 (7.2)	20 (5.6)	27 (9.3)
Menopause status, n (%)			
Natural	570 (87.4)	322 (89.4)	248 (84.9)
Premenopausal/Perimenopausal/Induced menopause	82 (12.6)	38 (10.6)	44 (15.1)
ECOG PS at palbociclib initiation, n (%)			
0	200 (30.7)	107 (29.7)	93 (31.8)
1	339 (52.0)	200 (55.6)	139 (47.6)
2	85 (13.0)	42 (11.7)	43 (14.7)
≥3	28 (4.4)	11 (3.1)	17 (5.8)
Stage at ABC/MBC, n (%)			
Locoregionally advanced (IIIb, IIIc)	135 (20.7)	67 (18.6)	68 (23.3)
Metastatic (stage IV)	517 (79.3)	293 (81.4)	224 (76.7)
Occurrence of breast cancer, n (%)			
Recurrent	367 (56.3)	127 (35.3)	240 (82.2)
De novo	285 (43.7)	233 (64.7)	52 (17.8)
Metastatic sites, n (%)[b]			
No. Of patients	517	293	224
Visceral[a]	240 (46.4)	147 (50.2)	93 (41.5)
Non-visceral	277 (53.6)	146 (49.8)	131 (58.5)
Bone only	240 (46.4)	127 (43.3)	113 (50.4)
Lung, bilateral	87 (16.8)	52 (17.7)	35 (15.6)
Lymph nodes, regional	82 (15.9)	51 (17.4)	31 (13.8)
Lymph nodes distal	64 (12.4)	40 (13.7)	24 (10.7)
Prior therapy for EBC, n (%)			
No. Of patients	367	127	240
Surgery	271 (73.8)	105 (82.7)	166 (69.2)
Adjuvant endocrine therapy	264 (71.9)	57 (44.9)	207 (86.3)
Radiotherapy	254 (69.2)	92 (72.4)	162 (67.5)
Adjuvant chemotherapy	135 (36.8)	63 (49.6)	72 (30.0)
Neoadjuvant therapy	25 (6.8)	10 (7.9)	15 (6.3)
Unknown	10 (2.7)	5 (3.9)	5 (2.1)
Prior therapy for ABC/MBC, n (%)			
No. Of patients	217	31	186
Endocrine	153 (70.5)	0	153 (82.3)
Chemotherapy	43 (19.8)	28 (90.3)	15 (8.1)
Targeted	21 (9.7)	3 (9.7)	18 (9.7)
Lines of treatment for ABC/MBC, n (%)			
No. Of patients	652	360	292
1	376 (57.7)	287 (79.7)	89 (30.5)
2	227 (34.8)	60 (16.7)	167 (57.2)
3+	49 (7.5)	13 (3.6)	36 (12.3)

AbbreviationsABC, advanced breast cancer; AI, aromatase inhibitor; EBC, early-stage breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; MBC, metastatic breast cancer; SD, standard deviation.

[a] Patients with stage IV/MBC defined as having metastases to the lung, brain, liver or ovaries.

[b] Data for patients with metastatic disease only.

palbociclib + fulvestrant patients had experienced a natural menopause with the remaining patients being induced, premenopausal or perimenopausal. Patients' prior therapy for early-stage breast cancer and ABC/MBC are shown in Table 2.

3.2. Treatment patterns

At the time of data extraction, palbociclib treatment was ongoing in 518 patients (79.4%), 284 (78.9%) of those in the palbociclib + AI group and 234 (80.1%) in the palbociclib + fulvestrant group.

3.2.1. Palbociclib + AI

The mean (SD) time from diagnosis of ABC/MBC to palbociclib initiation was 4.3 (12.0) months; 303 patients (84.2%) initiated palbociclib treatment within 12 months of ABC/MBC diagnosis. All patients receiving palbociclib + AI did so as an initial endocrine-based therapy, per the labeled indication. Of these, 28 patients (8.6%) received chemotherapy as prior therapy in the advanced setting. The most commonly prescribed AIs were letrozole (n = 286; 79.4%), anastrozole (n = 55; 15.3%), and exemestane (n = 19; 5.3%).

The most common starting dose of palbociclib was 125 mg/d (n = 279; 77.5%) (Fig. 1). Dose adjustments were seen in 71 patients (19.7%), most frequently reduction from 125 mg/d to 100 mg/d (n = 41; 57.7%). Most patients (n = 60; 84.5%) only required one dose adjustment. Treatment was discontinued in 76 patients (21.1%), most frequently for disease progression (n = 56; 73.7%). The mean (SD) duration of palbociclib treatment among patients discontinuing treatment was 8.3 (4.2) months; the mean (SD) duration of palbociclib treatment for patients with ongoing treatment was 11.1 (5.1) months.

3.2.2. Palbociclib + fulvestrant

The mean (SD) time from diagnosis of ABC/MBC to initiation of palbociclib + fulvestrant was 11.4 (16.7) months; 163 patients (55.8%) initiated palbociclib + fulvestrant treatment within 12 months of ABC/MBC diagnosis. Patients received palbociclib + fulvestrant in the first (n = 106; 36.3%), second (n = 162; 55.5%), and third or later (n = 24; 8.2%) lines.

The most common starting dose of palbociclib was 125 mg/d (n = 213; 72.9%) (Fig. 1); patients were also initiated on 100 mg and 75 mg. Dose adjustments were seen in 42 patients (14.4%), most frequently from 125 mg/d to 100 mg/d (n = 25; 59.5%); 34 patients (80.9%) only required one dose adjustment.

Treatment was discontinued in 58 patients (19.9%), most commonly because of was disease progression (n = 28; 48.3%). The mean (SD) duration of therapy among patients who discontinued treatment was 3.7 (3.5) months; among those in whom treatment was ongoing, the median duration of treatment was 7.4 (3.2) months.

3.3. Outcomes

3.3.1. Palbociclib + AI

At the time of data collection, after a mean follow-up of 9.9 months (SD 5.2), 56 patients receiving palbociclib + AI (15.6%) had disease progression. The 12-month progression-free rate was 84.1%; 64.3% of patients remained progression-free at 24 months (Fig. 2A). At the time of data collection, 21 of 358 evaluable patients (5.9%) had died; 12- and 24-month survival rates were 95.1% and 90.1%, respectively (Fig. 2B).

Objective responses, calculated based on the physician's assessments as recorded in patient charts, were achieved in 283 patients (79.5%), including CR in 39 patients (11.0%) and PR in 244 (68.5%) (Table 3). The mean (SD) time to CR after palbociclib initiation was 6.0 (3.9) months and the mean time (SD) to PR was 3.9 (2.0) months. The CBR, excluding patients censored for having stable disease for <24 weeks, was 93.8%. When stable disease-

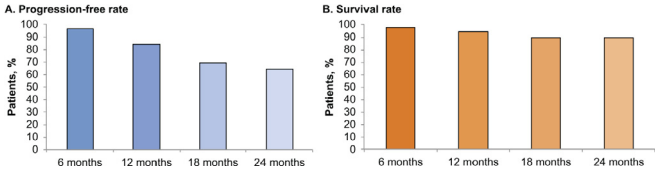

Fig. 2. Kaplan-Meier progression-free (A) and survival (B) rates in patients treated with palbociclib + aromatase inhibitor.

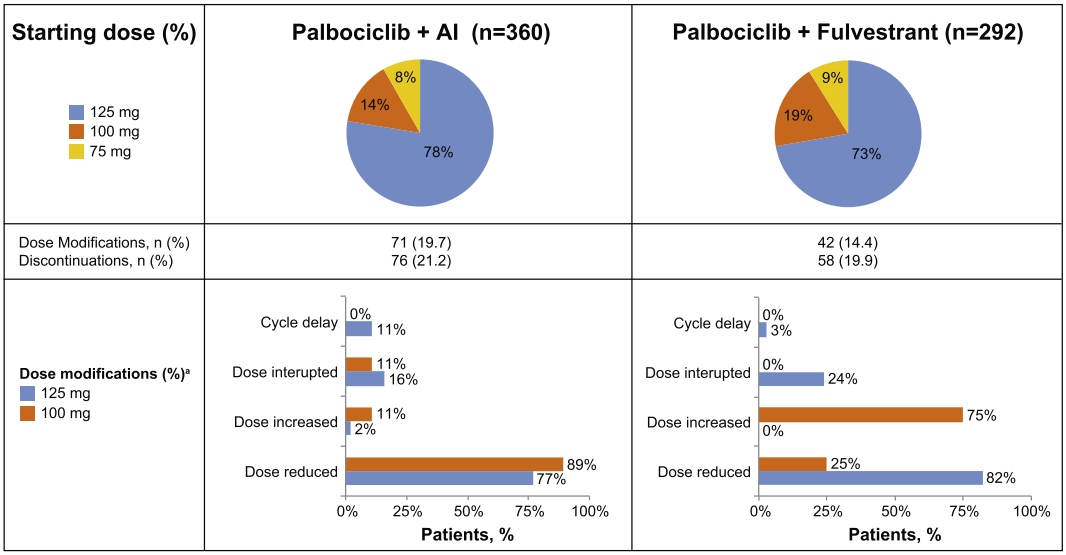

Fig. 1. Dose adjustments in patients treated with palbociclib + AI or palbociclib + fulvestrant. AI, aromatase inhibitor. [a]No dose modifications were required by patients on a starting dose of 75 mg.

Table 3
Response to palbociclib treatment.

	Overall (n = 652)	Palbociclib + AI (n = 360)	Palbociclib + fulvestrant			
			All (n = 292)	First line (n = 106)	Second line (n = 162)	Third line (n = 22)
Best response, n (%)						
No. Of patients	637	356	281	104	154	21
Complete response	63 (9.9)	39 (11.0)	24 (8.5)	8 (7.7)	14 (9.1)	2 (9.5)
Partial response	428 (67.2)	244 (68.5)	184 (65.5)	64 (61.5)	104 (67.5)	15 (71.4)
Stable disease ≥24 weeks	82 (12.9)	51 (14.3)	31 (11.0)	15 (14.4)	15 (9.7)	1 (4.8)
Stable disease <24 weeks	14 (2.2)	5 (1.4)	9 (3.2)	5 (4.8)	3 (1.9)	1 (4.8)
Objective response rate, n (%)	491 (77.1)	283 (79.5)	208 (74.0)	72 (69.2)	118 (76.6)	17 (81.0)
Clinical benefit rate, n (%)						
Upper bound[a]	596 (93.6)	334 (93.8)	262 (93.2)	96 (92.3)	146 (94.8)	19 (90.5)
Lower bound[b]	573 (90.0)	334 (93.8)	239 (85.1)	87 (83.7)	133 (86.4)	18 (85.7)

Data were censored for clinical benefit rate if a patient was still receiving palbociclib but had <24 weeks' data available and no evidence of CR, PR, or progression.; Abbreviation: AI, aromatase inhibitor.
[a] Includes stable disease censored.
[b] Excludes stable disease censored.

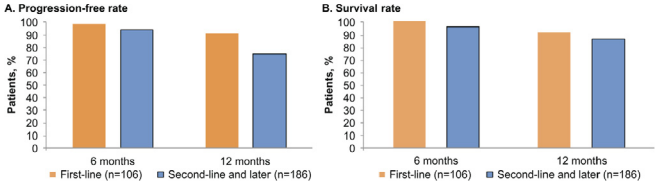

Fig. 3. Kaplan-Meier progression-free (A) and survival (B) rates in patients treated with palbociclib + fulvestrant.

censored patients were included, the CBR was 93.8%.

3.3.2. *Palbociclib + fulvestrant*

At the time of data collection, 28 palbociclib + fulvestrant patients (9.6%) had disease progression. The 12-month progression-free rate was 79.8% overall, 89.6% for first-line patients, and 73.7% in second- or later-line patients (Fig. 3A). At the time of data collection, 15 patients (5.1%) had died. The 12-month survival rate was 87.9% overall, 91.1% for first-line patients and 85.9% in second- or later-line patients (Fig. 3B). Progression-free and survival rates were not available beyond 12 months as a result of the limited time on treatment in this group.

Objective responses were reported in 208 of 281 evaluable patients (74.0%) in the palbociclib + fulvestrant group, including CR in 24 patients (8.5%) and PR in 184 patients (65.5%) (Table 3). The mean (SD) time to CR after palbociclib initiation was 3.8 (1.7) months and the mean (SD) time to PR was 3.5 (1.6) months. The CBR, excluding patients censored for having stable disease, was 93.2%; when censored patients were included, the CBR was 85.1%.

4. Discussion

The greatest challenge faced by physicians managing patients with HR+/HER2- ABC/MBC is the emergence of resistance to endocrine therapy. The introduction of new agents, including the novel selective CDK4/6 inhibitor palbociclib, is a major advance in the treatment of ABC/MBC. Palbociclib in combination with an AI or fulvestrant is a first-in-class treatment in this setting, with demonstrated efficacy in clinical trials [6–9]. To aid understanding of the use of palbociclib-based combinations and associated clinical outcomes in the real-world setting, the IRIS study extracted data from the medical records of patients treated with palbociclib in community and academic practices in the US.

Letrozole was the most commonly used partner therapy with palbociclib for initial endocrine-based treatments in this study, reported for 79.4% of patients who received an AI; other AIs used in combination with palbociclib included anastrozole (15.3%) and exemestane (5.3%). Most patients (75.5%) started treatment on palbociclib 125 mg/d as recommended in the US prescribing information [5]; the majority of patients (83.9%) remained on this dose. Overall, dose adjustments were required in only 17.3% of patients overall, 19.7% of palbociclib + AI patients, and 14.4% of palbociclib + fulvestrant patients. These dose-adjustment rates are lower than observed in palbociclib + letrozole-treated patients in the PALOMA-2 trial, 36% of whom had palbociclib dose reductions [6], and in the palbociclib + fulvestrant arm of the PALOMA-3 trial, in which 34% of patients had dose reductions, 36% had cycle delays, and 54% had dose interruptions [10]. It should be noted, however, that the PALOMA trials mandated that all patients start on a palbociclib dose of 125 mg/d, which may have affected the difference in dose adjustments observed between the PALOMA trials and the real-world setting. At the time of data extraction, 20.6% of patients had discontinued palbociclib, of whom 62.6% discontinued as a result of disease progression. In the clinical-trial setting, 39%, and 37% of palbociclib-treated patients in PALOMA-2, and -3, respectively, discontinued treatment because of disease progression [6,9]. The difference between studies could be due to the length of follow-up of IRIS and the randomized controlled trials.

Among patients undergoing first-line treatment with palbociclib + AI for ABC/MBC, objective responses were achieved in 79.5% of patients, and 93.8% achieved clinical benefit. These results, which compare favorably with ORR and CBR data from the PALOMA-2 study (ORR, 42%; CBR, 85%) [9], could include confirmed or unconfirmed responses as extraction of evidence of radiological confirmation was not requested as part of the IRIS case report form. After 1 year, 84.1% of palbociclib + AI patients were progression-free and 95.1% were alive; after 2 years, 64.3% of patients were progression-free and 90.1% were alive. As limited survival data have been published for palbociclib-treated US patients with ABC/MBC to date, the results of the present study provide valuable information relating to the use of palbociclib + AI in patients treated in real world clinical practice.

In the group of patients who had progressed on prior endocrine therapy, treatment with palbociclib + fulvestrant resulted in an ORR of 74.0% and a CBR of 85.1%. After 1 year, 79.8% of palbociclib + fulvestrant-treated patients overall were progression-free and 87.9% were alive. Promising survival data were observed for patients undergoing both first- and later-line treatment with palbociclib plus fulvestrant, with 12-month progression-free and survival rates of 73.7% and 85.9%, respectively, in the latter. These data represent, to the best of our knowledge, the first real-world evidence for the effectiveness of palbociclib + fulvestrant outside

of clinical trials.

Some differences between the real-world patients in IRIS and those in the clinical trials that tested palbociclib should be considered. IRIS included patients with poor ECOG PS, who comprise a considerable proportion of the population seen in clinical practice but are underrepresented in clinical trials. Overall, 16.7% of patients in IRIS had an ECOG PS of 2 or 3, with a higher proportion in the palbociclib + fulvestrant group (19.2% vs 14.8% for palbociclib + AI). This is in line with the more advanced disease typically seen in patients treated with palbociclib + fulvestrant.

Limitations of this study should be considered. Data were only collected by physicians willing to participate in the study, introducing a potential selection bias. Data were only collected for patients initiating treatment ≥6 months before chart abstraction for palbociclib + AI and ≥3 months for palbociclib + fulvestrant. The palbociclib + fulvestrant combination was only approved in the US in February 2016; consequently, 18- and 24-month data were not available for Kaplan-Meier analysis for this group. To eliminate potential selection bias, physicians were asked to select consecutive patients in line with the index date. Despite these limitations, the current study provides much needed insight into the real-world use of palbociclib in US patients with MBC/ABC.

In conclusion, the IRIS study provides first-of-its-kind information regarding real-world treatment patterns and clinical outcomes associated with palbociclib in combination with an AI or fulvestrant in patients with HR+/HER- ABC/MBC in the US.

Declaration of interests statement

Gavin Taylor-Stokes, John Waller, Katie Gibson, and Gary Milligan are salaried employees of Adelphi Real World who received funding to conduct this study. Debanjali Mitra and Shrividya Iyer are employees of and own stock in Pfizer Inc.

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Conflicts of interest

Gavin Taylor-Stokes, John Waller, Katie Gibson, and Gary Milligan are salaried employees of Adelphi Real World who received funding to conduct this study. Debanjali Mitra and Shrividya Iyer are employees of and own stock in Pfizer Inc.

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