Retrospective Assessment of Treatment Patterns and Outcomes Associated With Palbociclib Plus Letrozole for Postmenopausal Women With HR+/HER2– Advanced/Metastatic Breast Cancer Enrolled in an Expanded Access Program in the United States

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BACKGROUND

- Postmenopausal women with hormone receptor-positive (HR+), human epidermal growth factor receptor-negative (HER2-) advanced or metastatic breast cancer (ABC/MBC) have traditionally been treated with endocrine-based systemic therapy in the absence of visceral crisis.
- Palbociclib was the first CDK 4/6 inhibitor approved by the United States (US) Food and Drug Administration in 2015 for use in combination with letrozole (P + L) as initial endocrine-based therapy.
- Prior to approval, an expanded access program (EAP) was made available in the US for the use of P + L across all lines of therapy. The EAP enrolled a substantial cohort of heavily pretreated patients.
- This is a retrospective, long term follow-up of patients from the EAP, focusing on late-line, heavily pre-treated patients who continued their P + L treatment in the real-world setting.[1]

OBJECTIVE

- The objective of this retrospective follow-up study was to evaluate long-term treatment patterns and clinical outcomes for a subset of sites and patients who began P + L treatment on the EAP and continued treatment in the real world after the close of the EAP.

METHODS

Data Source

- Data were obtained from medical records of patients originally enrolled in the palbociclib EAP study, which covered 238 patients and spanned 18 sites across the US.
- Of the original 18 sites, 6 sites contributed data for 126 patients for this follow-up study.
- All data were entered into an electronic case report form by clinical research staff at the participating sites.

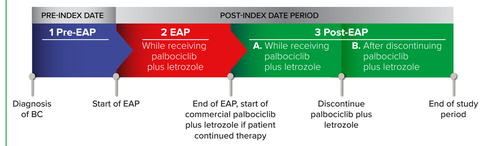
Patient Selection

- All patients enrolled in the original EAP study were eligible for inclusion in the current study.

Study Measures

- Patient characteristics included demographics, history of comorbidities, stage at initial breast cancer diagnosis, performance status, and sites of metastasis.
- All cancer-directed treatments, total number of lines of therapy, and duration of each treatment line for the pre- and post-EAP periods were documented.

Figure 1. Study Design



Period 1: Starting with the patient's initial diagnosis of breast cancer through the study index date (defined as enrollment date into the EAP).

Period 2: Starting with the patient's enrollment in the EAP (index date) through the patients' disenrollment in the EAP.

Period 3: Starting with the patient's disenrollment from the EAP through the end of follow-up or death, whichever occurs first. The post-EAP period may be composed of time periods on multiple therapies including those after discontinuation of palbociclib plus letrozole.

A: A period while the patient continued on commercially available palbociclib plus letrozole.

B: A period after discontinuation of palbociclib plus letrozole.

- The following clinical outcomes were assessed for the overall cohort and stratified by prior treatments (endocrine therapy or chemotherapy) received in the ABC/MBC setting:
  - Best physician-assessed response to P + L therapy: Response was based on tumor assessments carried out per local practice and were not based on RECIST criteria. Response categories included:
    - Estimated Objective Response (OR): Complete response + Partial response
    - Estimated Clinical Benefit Rate (CBR): Complete response + Partial response + Stable Disease for ≥ 24 weeks.
  - Progression-free survival (PFS) for P + L therapy, calculated as time (months) from P + L initiation to first clinician-documented progression event, start of a new line of therapy (if patients discontinued P + L due to "progression" as the reason for discontinuation), or death due to any cause, whichever occurred first. If a patient died or started a new therapy line on a date more than 24 weeks after final palbociclib dose, the patient was censored at that date (last palbociclib dose + 24 weeks) and was not counted as having a progression event.
  - Time to death (overall survival [OS]) for P + L therapy, calculated as time (months) from P + L initiation to the earlier of death or end of follow-up.

Data Analysis

- Descriptive statistics were used to document baseline patient characteristics and study outcomes.
- Overall use of cancer-directed treatments and treatment characteristics (e.g., treatment composition) were analyzed by time periods.
- Median PFS and OS and landmark analyses of progression-free rates and survival rates are described using the Kaplan-Meier method.
- All analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc.; 2011).

RESULTS

Patient Demographics and Baseline Clinical Characteristics

- The sample was predominantly white (83%), with a mean age at EAP enrollment of 62.5 years (standard deviation [SD]: 12.2 years) (Table 1).
- More than a quarter (25.4%) of patients had metastatic disease at initial diagnosis; more than 70% were ER+ or PgR+ (Table 1).
- 72% of patients had visceral metastasis at EAP enrollment.
- 38.1% of patients were alive at last available medical record (Table 1).
- More than 90% of patients had an ECOG status of 0 or 1 at EAP enrollment, indicating a favorable functional capacity for the study sample as a whole prior to first palbociclib dose.
- The most common comorbidities present at EAP enrollment were hypertension (27.8%) and diabetes (5.6%), while 54.8% had none of the comorbidities examined.

Treatment History Prior to EAP Enrollment

- Almost 90% of patients included received some form of cancer-directed treatment prior to EAP enrollment; the most common (86.5%) treatment modality pre-EAP enrollment was endocrine therapy (with or without chemotherapy), with only 2.4% receiving chemotherapy only (Figure 2).
- Most patients had three or more lines of systemic treatment (58.7%) in the ABC/MBC setting before EAP enrollment. Of the total sample, 88.9% received at least one systemic line of therapy prior to EAP enrollment, 94 (74.6%) received at least two prior lines of therapy, 74 (58.7%) received at least three prior lines of therapy, and 47 (37.3%) received at least four prior lines of therapy.

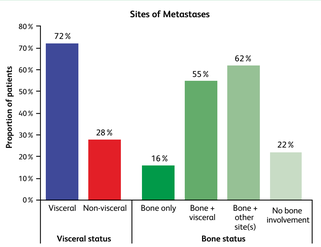
Clinical Outcomes

- CBR was higher for patients with no prior endocrine therapy in the ABC/MBC setting prior to EAP enrollment (52.9%) compared with those who did (30.3%). Likewise, patients who did not receive chemotherapy prior to EAP enrollment had a higher CBR (48.8%) than those who did (25.9%) (Figures 3 and 4).
- Median (95% CI) PFS was 4.4 (3.5-5.5) months for patients with prior endocrine therapy in the ABC/MBC setting and 3.9 (2.5-5.1) months for patients with prior chemotherapy (Table 2).
- 12- and 24-month OS rates among patients with prior endocrine therapy were 65% and 40%, respectively, while they were 63% and 32%, respectively, among patients with prior chemotherapy (Table 2).

Table 1. Baseline Patient and Clinical Characteristics

Total patients, n (%)	**126**	**100.0%**
Age at EAP enrollment, years		
Mean (SD)	62.5	12.2
Median	62.5	
Min, Max	37	89
Ethnic origin, n (%)		
White	105	83.3%
Black	11	8.7%
Other	5	4.0%
Unknown	5	4.0%
Disease stage at initial breast cancer diagnosis, n (%)		
Local	46	36.5%
Regional	40	31.7%
Metastatic	32	25.4%
Unknown	8	6.3%
Tumor grade at initial breast cancer diagnosis, n (%)		
Grade 1	8	6.3%
Grade 2	51	40.5%
Grade 3	34	27.0%
Unknown	33	26.2%
Time from initial breast cancer diagnosis to first diagnosis of or progression to metastatic disease, months (among those diagnosed with early stage disease) (N = 94)		
Mean (SD)	103.3	86.0
Median	81.8	
Min, Max	1.0	407.2
Duration (months) of follow-up from initial breast cancer diagnosis (among those with early stage diagnosis) (N = 94)		
Mean (SD)	160.5	101.6
Median	144.5	
Min, Max	23.5	465.7
Vital status at study completion (n, %)		
Alive	48	38.1%
Deceased	59	46.8%
Unknown	19	15.1%

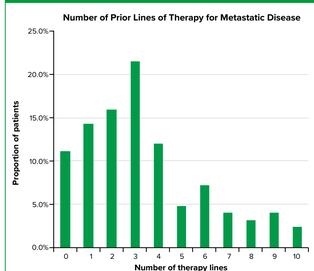
Figure 2. Sites of Metastases at EAP Enrollment



Most Frequently Occurring Sites

Site	N	%
Bone	98	77.8%
Liver	58	46.0%
Lymph nodes	55	43.7%
Lung	32	25.4%
Pleura	23	18.3%
Skin/soft tissue	12	9.5%
Brain	8	6.3%
Peritoneal	6	4.8%
Adrenal	2	1.6%
Chest wall	2	1.6%
Mediastinum	2	1.6%
Spleen	2	1.6%

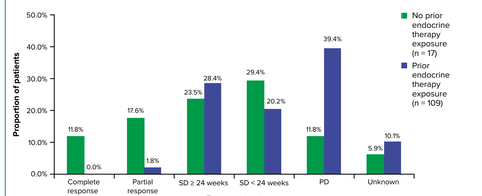
Figure 3. Pre-EAP Treatment Patterns



Types of Pre-EAP Treatments Received in Metastatic Setting

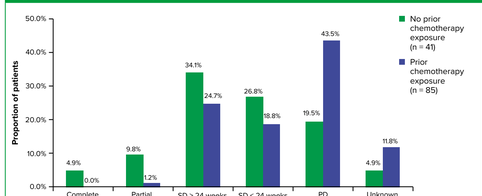
Therapies	N	%
Chemotherapy only	3	2.4%
Endocrine therapy only	27	21.4%
Both chemotherapy and endocrine therapy	82	65.1%
No treatment	14	11.1%
Regimens containing		
Anastrazole	53	42.1%
Letrozole	41	32.5%
Tamoxifen	42	33.3%
Exemestane	68	54.0%
Fulvestrant	84	66.7%

Figure 4. Best Clinical Response to Treatment by Prior Endocrine Exposure



Best Response, n (%)	No Prior Endocrine Therapy (n = 17)	Prior Endocrine Therapy (n = 109)
OR	5 (29.4%)	2 (1.8%)
CBR	9 (52.9%)	33 (30.3%)

Figure 5.Best Clinical Response to Treatment by Prior Chemotherapy Exposure



Best Response, n (%)	No Prior Chemotherapy Exposure (n = 41)	Prior Chemotherapy Exposure (n = 85)
OR	6 (14.6%)	1 (1.2%)
CBR	20 (48.8%)	22 (25.9%)

Table 2. Survival Outcomes for P + L Therapy

PFS, months	No Prior Endocrine Therapy Exposure (N = 17)	Prior Endocrine Therapy Exposure (N = 109)	No Prior Chemotherapy Exposure (N = 41)	Prior Chemotherapy Exposure (N = 85)
n (%) of patients with event	11 (64.7%)	87 (79.8%)	29 (70.7%)	69 (81.2%)
Median PFS (95% CI)	8.6 (3.5-NE)	4.4 (3.5-5.5)	7.0 (4.2-14.7)	3.9 (2.5-5.1)
PFS rates via Kaplan-Meier estimation				
12-month PFS rate	47.1%	23.7%	40.4%	19.8%
24-month PFS rate	32.3%	7.0%	24.1%	–
OS, months				
n (%) of patients with death event	6 (35.3%)	53 (48.6%)	14 (34.1%)	45 (52.9%)
Median time to death among those who died	6.3	7.0	6.9	7.7
Median OS (95% CI)	NE (7.0-NE)	19.8 (13.9-NE)	NE (19.8-NE)	14.9 (12.1-23.5)
12-month OS rate	70.6%	65.4%	72.5%	62.8%
24-month OS rate	61.8%	39.8%	63.1%	31.8%

NE = not estimable.

DISCUSSION

- Patients in this study were heavily pretreated in the ABC/MBC setting before starting P + L treatment. The OR rates and CBRs reported here demonstrate clinical benefit even in this heavily pretreated population.
- Twelve- and 24-month PFS rates for patients with prior endocrine exposure in the ABC/MBC setting were 23.7% and 7.0%, respectively; 12- and 24-month response rates for no prior endocrine exposure were 47.1% and 32.3%, respectively. Median OS was 19.8 months in patients with prior endocrine therapy and 14.9 months in patient with prior chemotherapy. These findings highlight the potential benefit of treatment with palbociclib combination therapy in HR+/HER2– MBC even in later lines of therapy.

CONCLUSIONS

- Consistent with clinical experience, patients with fewer prior treatments for MBC generally obtained better outcomes. Nevertheless, even in heavily pretreated patients, clinical benefit may be derived with P + L.
- These findings further highlight the importance and potential benefit of treatment with palbociclib combination therapy in HR+/HER2– ABC/MBC.

REFERENCES

1. Stearns V et al. Abstract P4-13-05. Presented at the 38th Annual CTRC-AACR San Antonio Breast Cancer Symposium; December 8-12, 2015; San Antonio, TX.

DISCLOSURES

This study was sponsored by Pfizer. KLD and SN are employees of RTI Health Solutions, who were paid consultants to Pfizer in connection with the development of this poster.

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