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Breast Cancer

Long-Term Pooled Safety Analysis of Palbociclib in Combination with Endocrine Therapy for Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Updated Analysis with up to 5 Years of Follow-Up

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Long-term safety • Pooled safety • Palbociclib • Advanced breast cancer • HR+/HER2−

Abstract

Background. Previous studies demonstrated the tolerability of palbociclib plus endocrine therapy (ET). This analysis evaluated safety based on more recent cutoff dates and a longer palbociclib treatment exposure.

Patients and Methods. Data were pooled from three randomized studies of patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2−) advanced breast cancer (ABC), including postmenopausal women who had not received prior systemic treatment for advanced disease (PALOMA-1/-2) and pre- and postmenopausal women who had progressed on prior ET (PALOMA-3).

Results. Updated cutoff dates were December 21, 2017 (PALOMA-1), May 31, 2017 (PALOMA-2), and April 13, 2018 (PALOMA-3). Total person-years of treatment exposure were 1,421.6 with palbociclib plus ET (n = 872) and 528.4 with ET (n = 471). Any-grade neutropenia and infections were more frequent with palbociclib plus ET (82.1% and 59.2%, respectively) than with ET (5.1% and 39.5%). The hazard ratios were 1.6 (p = .0995) for grade 3/4 infections, 1.8 (p = .4358) for grade 3/4 viral infections, 1.4 (p = .0001) for infections, and 30.8 (p < .0001) for neutropenia. Febrile neutropenia was reported in 1.4% of patients receiving palbociclib plus ET. Cumulative incidence of all-grade hematologic adverse events in both arms peaked during the first year of treatment and plateaued over the 5 subsequent years. Interstitial lung disease was reported in 13 patients receiving palbociclib plus ET and 3 receiving ET.

Conclusion. This 5-year, long-term analysis demonstrated that palbociclib plus ET has a consistent and stable safety profile and is a safe treatment for patients with HR+/HER2− ABC. ***The Oncologist*** 2021;25:1–7

Implications for Practice: Several treatments for patients with breast cancer are associated with long-term or latent adverse events. This long-term, 5-year analysis demonstrated that palbociclib plus endocrine therapy has a consistent and stable safety profile without cumulative or delayed toxicities. These results further support palbociclib plus endocrine therapy as a safe and manageable treatment in clinical practice for patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer.

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Introduction

Palbociclib, a cyclin-dependent kinase (CDK) 4/6 inhibitor, is approved in combination with endocrine therapy (ET) for the treatment of patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2−) advanced breast cancer (ABC) [1]. The safety and efficacy of palbociclib have been demonstrated in women with HR+/HER2− ABC in the phase II PALOMA-1 and phase III PALOMA-2 and PALOMA-3 clinical studies [2–4], significantly improving median progression-free survival (PFS) when combined with letrozole or fulvestrant compared with letrozole alone or placebo plus letrozole, or placebo plus fulvestrant, respectively [2, 5, 6]. Although palbociclib combination therapies with either letrozole or fulvestrant in PALOMA-1 or PALOMA-3 were associated with longer median overall survival (OS) compared with letrozole alone or placebo plus fulvestrant, respectively, the results were not statistically significant [7, 8].

Introduction of new treatments has improved outcomes in patients with ABC [9, 10]. Therefore, treatments should focus not only on survival but also on quality of life (QoL). Anticancer drug–related adverse events (AEs) negatively affect QoL [11, 12], which should be taken into consideration when choosing treatments. Although one goal of treating patients with ABC is to minimize AEs associated with treatment, long-term AEs that persist or latent AEs that may not present until several years after completion of treatments are both commonly reported [13]. Additionally, real-world evidence revealed that treatment with certain CDK4/6 inhibitors is associated with increased risk for interstitial lung disease (ILD) and venous thromboembolism [14, 15], with the latter associated with shorter PFS and OS [15]. Moreover, a retrospective pharmacovigilance analysis of data from the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS) showed that 0.6% of the 25,503 cases of ILD reported in FAERS were associated with CDK4/6 inhibitors [16].

Given the long-term disease control provided by palbociclib therapy, these issues are especially important to analyze. A previous pooled analysis of data from the PALOMA studies (data cutoffs: PALOMA-1, January 2, 2015; PALOMA-2, February 26, 2016; PALOMA-3, July 31, 2015) demonstrated the tolerability of palbociclib [17]. The most commonly reported AEs associated with palbociclib treatment were hematologic [17]. The current analysis evaluated the safety profile of palbociclib based on data with more recent cutoff dates from the PALOMA clinical studies and reports results from longer treatment exposure.

Materials and Methods

Study Design

The study designs of the 3 PALOMA studies have been described in detail previously [2–4]. Briefly, PALOMA-1 (NCT00721409) was a phase II, open-label study that randomized women 1:1 between December 2009 and May 2012 to receive either oral palbociclib (125 mg/day, 3 weeks on/1 week off treatment for a 3/1 schedule) plus continuous oral letrozole (2.5 mg/day; *n* = 84), or continuous oral letrozole alone (*n* = 81). PALOMA-2 (NCT01740427), a phase III, double-blind, placebo-controlled study, randomized women 2:1 between February 2013 and July 2014 to receive either oral palbociclib (125 mg/day, 3/1 schedule) plus continuous oral letrozole (2.5 mg/day; *n* = 444) or matching placebo plus letrozole (*n* = 222). Women from the phase III, double-blind, placebo-controlled PALOMA-3 study (NCT01942135) were randomized 2:1 between October 2013 and August 2014 to receive either oral palbociclib (125 mg/day, 3/1 schedule) plus fulvestrant (500 mg, intramuscular injection, every 14 days for the first three injections, then every 28 days thereafter; *n* = 347) or placebo plus fulvestrant (*n* = 174).

The PALOMA studies were conducted in accordance with the International Council for Harmonisation and Good Clinical Practice standards; patients provided written informed consent before the initiation of study procedures.

Patients

Eligible patients from PALOMA-1 and PALOMA-2 were postmenopausal women with estrogen receptor-positive/HER2− ABC who had not received prior systemic treatment for ABC. PALOMA-3 enrolled women with HR+/HER2− ABC regardless of menopausal status whose disease had progressed on prior ET.

Safety Assessments and Analysis

Using the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (PALOMA-1) and version 4.0 (PALOMA-2 and -3), the severity of all-causality AEs was recorded. For all trials, laboratory analyses were performed every 2 weeks during the first two cycles and then at the start of each subsequent cycle. Physical examinations were conducted at screening and day 1 of each cycle. AEs were reported from the time informed consent was provided until ≥28 days after the last treatment dose and before initiation of new anticancer treatment, or until resolution or characterization of all AEs as chronic/stable (PALOMA-1), whichever occurred later [17]. This analysis reported the incidence rate of selected AEs per person-year of treatment exposure and the cumulative incidence of selected AEs at 1, 2, 3, 4, and 5 years (all-grade and grade 3/4). Reporting treatment duration–adjusted incidence rates per person per year analysis adjusts for the duration of treatment exposure to the risk for developing AEs. Serious AEs were also evaluated.

Cases of ILD were identified based on the narrow ILD standardized Medical Dictionary for Regulatory Activities query and included reported events of ILD, pneumonitis, pulmonary fibrosis, bronchiolitis, lung infiltration, and radiation pneumonitis. Cases with the following reported preferred terms (PTs) were considered to be cases of venous thromboembolism: pulmonary embolism, deep vein thrombosis, thrombophlebitis, postthrombotic syndrome, retinal vein occlusion, subclavian vein thrombosis, thrombophlebitis superficial, vena cava thrombosis, superior vena cava syndrome, and pelvic venous thrombosis. Pulmonary embolism was defined as any event with a reported PT of pulmonary artery thrombosis, pulmonary embolism, or pulmonary thrombosis.

Table 1. Treatment exposure in the PALOMA clinical trials

Parameter	PALOMA-1		PALOMA-2		PALOMA-3	
	PAL + LET (*n* = 83)	LET (*n* = 77)	PAL + LET (*n* = 444)	PBO + LET (*n* = 222)	PAL + FUL (*n* = 345)	PBO + FUL (*n* = 172)
Median number of cycles, *n*	15	8	21.5	15.0	12.0	5.0
Median treatment duration, days	421	231	610.5	413.0	330.0	137.0
Median average PAL or PBO daily dose, mg	125	N/A	125.0	125.0	125.0	125.0
Median relative dose, %	97.4	100	97.7	100	94.0	100
Subjects with no dose reduction, %	57.8	N/A	60.6	98.2	58.3	98.3
Subjects with at least one dose reduction, %	42.2	N/A	39.4	1.8	41.7	1.7

Abbreviations: FUL, fulvestrant; LET, letrozole; N/A, not applicable; PAL, palbociclib; PBO, placebo.

Results

For this updated analysis, the data cutoff dates were December 21, 2017 (PALOMA-1), May 31, 2017 (PALOMA-2), and April 13, 2018 (PALOMA-3). Of the patients who received palbociclib plus ET (*n* = 872), 36.0% were treated for ≥24 months, 22.4% for ≥36 months, 1.7% for ≥48 months, and 0.7% for ≥60 months, with the majority of these patients from PALOMA-2. In the ET group (*n* = 471), 20.2% of patients were treated for ≥24 months, 10.2% for ≥36 months, 0.8% for ≥48 months, and 0.4% for ≥60 months. Median treatment duration was 14.8 (range, 0–84.4) months and mean ± SD treatment duration was 19.6 ± 15.0 months for the palbociclib plus ET group and 2.9 (range, 0–74.7) months and 10.3 ± 13.2 months, respectively, for the ET group. The total person-years of treatment exposure were 1,421.6 in the palbociclib plus ET group and 528.4 in the ET group (Table 1).

In the palbociclib plus ET group, the all-grade AEs with the highest incidence rates per person-year of treatment exposure were neutropenia, leukopenia, and infections (Fig. 1). Any-grade neutropenia and infections were more frequent with palbociclib plus ET (82.1% and 59.2%, respectively) than in the ET group (5.1% and 39.5%); the hazard ratio was 30.8 ($p < .0001$) for neutropenia and 1.4 ($p = .0001$) for infections in the palbociclib plus ET group compared with the ET group. Cumulative 5-year grade 3/4 infections were reported in 6.4% of patients receiving palbociclib plus ET and 2.8% of patients receiving ET. After adjusting for treatment exposure, the incidence rates of grade 3/4 infections per person-year were 0.0521 with palbociclib plus ET and 0.0284 with ET (hazard ratio, 1.6; $p = .0995$) and of grade 3/4 viral infections per person-year were 0.0084 with palbociclib plus ET and 0.0038 with ET (hazard ratio, 1.8; $p = .4358$). The most common grade 3/4 infections were pneumonia and urinary tract infection with both palbociclib plus ET (0.92% and 0.92%, respectively) and ET (0.42% and 0.21%, respectively). The most common any-grade viral infections were nasopharyngitis and upper respiratory tract infection with both palbociclib plus ET (16.5% and 14.3%, respectively) and ET (9.8% and 8.5%, respectively). In the palbociclib plus ET group, the most common grade 3/4 viral infections were influenza (0.46%), bronchitis (0.34%), and upper respiratory tract infection (0.34%); in the ET group, hepatitis C and viral upper respiratory tract infection (0.21% each) were the most common.

Overlapping of viral infections and neutropenia occurred in 184 (22.1%) patients in the palbociclib plus ET group, with the majority (99.3%) of viral infections being grade 1/2 in severity (supplemental online Fig. 1). Overlapping grade 3/4 viral infections occurred in only 6 (0.7%) patients with neutropenia (all grades). The overlapping of viral infections (all grades) and grade 3/4 neutropenia occurred in 63 (10.5%) patients in the palbociclib plus ET group, with the majority (99.8%) of viral infections being grade 1/2 in severity. Overlapping grade 3/4 viral infections occurred in only one (0.2%) patient with grade 3/4 neutropenia.

The incidence rate of venous thromboembolism was 0.0225 per person-year with palbociclib plus ET and 0.0246 per person-year with ET (hazard ratio, 1.3; $p = .4458$); the incidence rate of pulmonary embolism was 0.0127 per person-year with palbociclib plus ET and 0.0132 per person-year with ET (hazard ratio, 1.4; $p = .5028$; Fig. 1). For diarrhea, the incidence rate per person-year was 0.3946 with palbociclib plus ET and 0.2820 with ET (hazard ratio, 1.2; $p = .1033$). The incidence rate for electrocardiogram QT prolongation was 0.0113 per person-year with palbociclib plus ET and 0.0076 per person-year with ET (hazard ratio, 1.1; $p = .9302$).

Febrile neutropenia was reported in 1.4% of patients in the palbociclib plus ET group, with an incidence rate of 0.0084 per person-year. No patients in the ET group experienced febrile neutropenia. The cumulative 5-year rate of lymphopenia in the palbociclib plus ET group was 2.8% (all grades) and 0.9% (grades 3/4); in the ET group, the rate was 0.6% (all grades) and 0% (grades 3/4). In both the palbociclib plus ET and ET groups, the cumulative incidence of all-grade hematologic AEs peaked during the first year of treatment and then plateaued over the 5 subsequent years (Fig. 2A, B). Similarly, the cumulative incidence of grade 3/4 AEs peaked during the first year of treatment in both the palbociclib plus ET and ET groups (Fig. 2C–F). When selected AEs were analyzed by 6-month intervals in the palbociclib plus ET group, the incidence of AEs were generally higher

AEs, incidence rate per person-year (absolute rate[a], %)	PAL+ET *n* = 872	ET *n* = 471	Hazard Ratio (95% CI)	*p* value
Neutropenia	4.58 (82.1)	0.12 (5.1)	30.8 (20.5–46.2)	<.0001
Thrombocytopenia	0.47 (22.3)	0.015 (1.1)	19.7 (8.1–47.9)	<.0001
Leukopenia	1.61 (48.6)	0.057 (3.6)	16.7 (10.3–27.2)	<.0001
Anemia	0.57 (29.6)	0.20 (11.0)	2.6 (1.9–3.4)	<.0001
Alopecia	0.18 (26.8)	0.097 (10.4)	2.3 (1.7–3.1)	<.0001
Stomatitis	0.49 (30.3)	0.16 (13.2)	2.2 (1.6–2.9)	<.0001
Rash	0.17 (18.1)	0.12 (9.3)	1.6 (1.2–2.3)	.0031
ALT increased	0.13 (10.6)	0.059 (5.1)	1.6 (1.0–2.6)	.0340
AST increased	0.13 (11.4)	0.080 (5.7)	1.5 (0.98–2.3)	.0591
Fatigue	0.48 (41.5)	0.41 (28.7)	1.4 (1.1–1.6)	.0030
Nausea	0.39 (36.0)	0.36 (26.3)	1.3 (1.0–1.6)	.0235
Diarrhea	0.39 (27.3)	0.28 (19.3)	1.2 (0.96–1.6)	.1033
Vomiting	0.23 (18.9)	0.21 (14.7)	1.1 (0.8–1.4)	.6832
Pyrexia	0.12 (13.2)	0.072 (6.8)	1.5 (1.0–2.3)	.0316
Decreased appetite	0.15 (17.4)	0.095 (9.1)	1.6 (1.2–2.3)	.0055
Infections[b]	1.07 (59.2)	0.87 (39.5)	1.4 (1.2–1.7)	.0001
Infections[c] (grade 3/4)	0.052 (6.8)	0.028 (3.0)	1.6 (0.91–2.9)	.0995
Pneumonia (grade 3/4)	0.0056 (0.92)	0.0057 (0.42)	1.7 (0.4–8.2)	.5033
Viral infections[c]	0.42 (36.1)	0.36 (23.6)	1.2 (0.97–1.5)	.0860
Viral infections[c] (grade 3/4)	0.0084 (1.2)	0.0038 (0.42)	1.8 (0.4–8.5)	.4358
Syncope	0.0098 (1.3)	0.011 (1.3)	0.7 (0.3–2.0)	.5281
ECG QT prolonged	0.011 (0.80)	0.0076 (0.64)	1.1 (0.3–4.1)	.9302
VTE	0.023 (3.2)	0.025 (1.9)	1.3 (0.6–2.9)	.4458
Pulmonary embolism	0.013 (1.8)	0.013 (1.1)	1.4 (0.5–3.9)	.5028

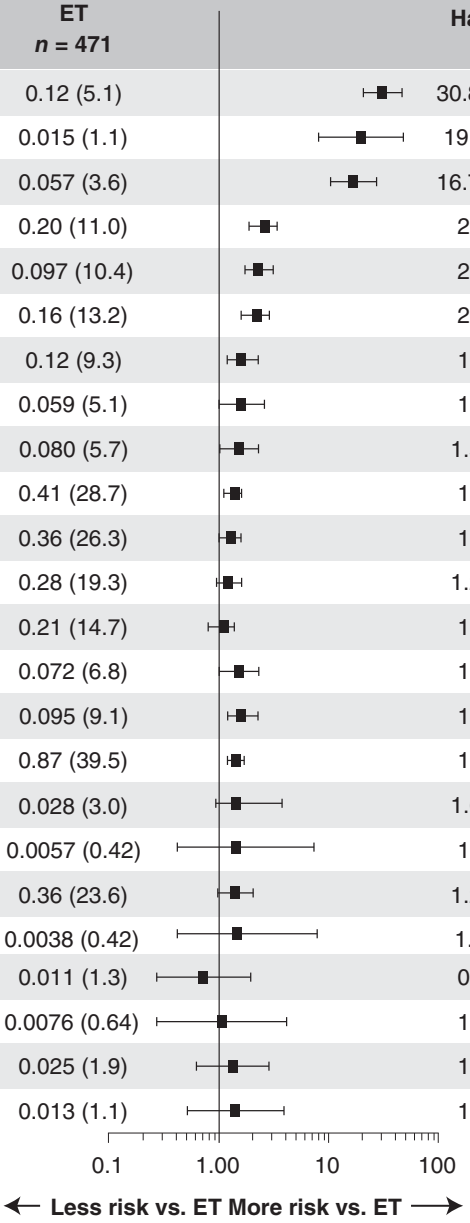

Figure 1. Incidence and absolute rates of selected AEs per person-year (all-grade AEs unless otherwise specified). [a]Absolute rates are not adjusted for treatment exposure. [b]Infections were defined as any event with a reported preferred term of the System Organ Class Infections and Infestations. [c]Viral infections were defined as any event with one of the following reported preferred terms: nasopharyngitis, upper respiratory tract infection, bronchitis, influenza, rhinitis, respiratory tract infections viral, viral infection, laryngitis, gastroenteritis viral, bronchiolitis, gastroenteritis norovirus, gastrointestinal viral infection, viral pharyngitis, viral upper respiratory tract infection, bronchitis viral, gastritis viral, croup infection, hepatitis C.
Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; ECG, electrocardiogram; ET, endocrine therapy; PAL, palbociclib; VTE, venous thromboembolism.

during the 0–6-month interval and fairly consistent over the subsequent 6-month intervals (supplemental online Fig. 2).

Adverse events that led to permanent study treatment discontinuation were reported in 11.1% of patients treated with palbociclib plus ET and 5.3% of patients receiving ET. The most common AEs leading to permanent discontinuation in ≥0.3% of patients in either treatment arm were neutropenia (1.7%), fatigue (0.8%), disease progression (0.7%), anemia (0.6%), increased alanine aminotransferase levels (0.5%), infections (0.5%), increased aspartate aminotransferase levels (0.3%), and diarrhea (0.3%) in the palbociclib plus ET group and infections (0.6%), ascites (0.4%), and fatigue (0.4%) in the ET group. Serious AEs (SAEs) were reported in 22.8% of patients in the palbociclib plus ET group and 15.5% of patients in the ET group. SAEs that led to permanent study treatment discontinuation were reported in 5.0% of patients receiving palbociclib plus ET and 3.6% of patients treated with ET. The most common SAEs leading to permanent discontinuation were disease progression (0.7%) in the palbociclib plus ET group and infections (0.6%) in the ET group.

Interstitial lung disease was reported in 13 patients receiving palbociclib plus ET, with one case reported as

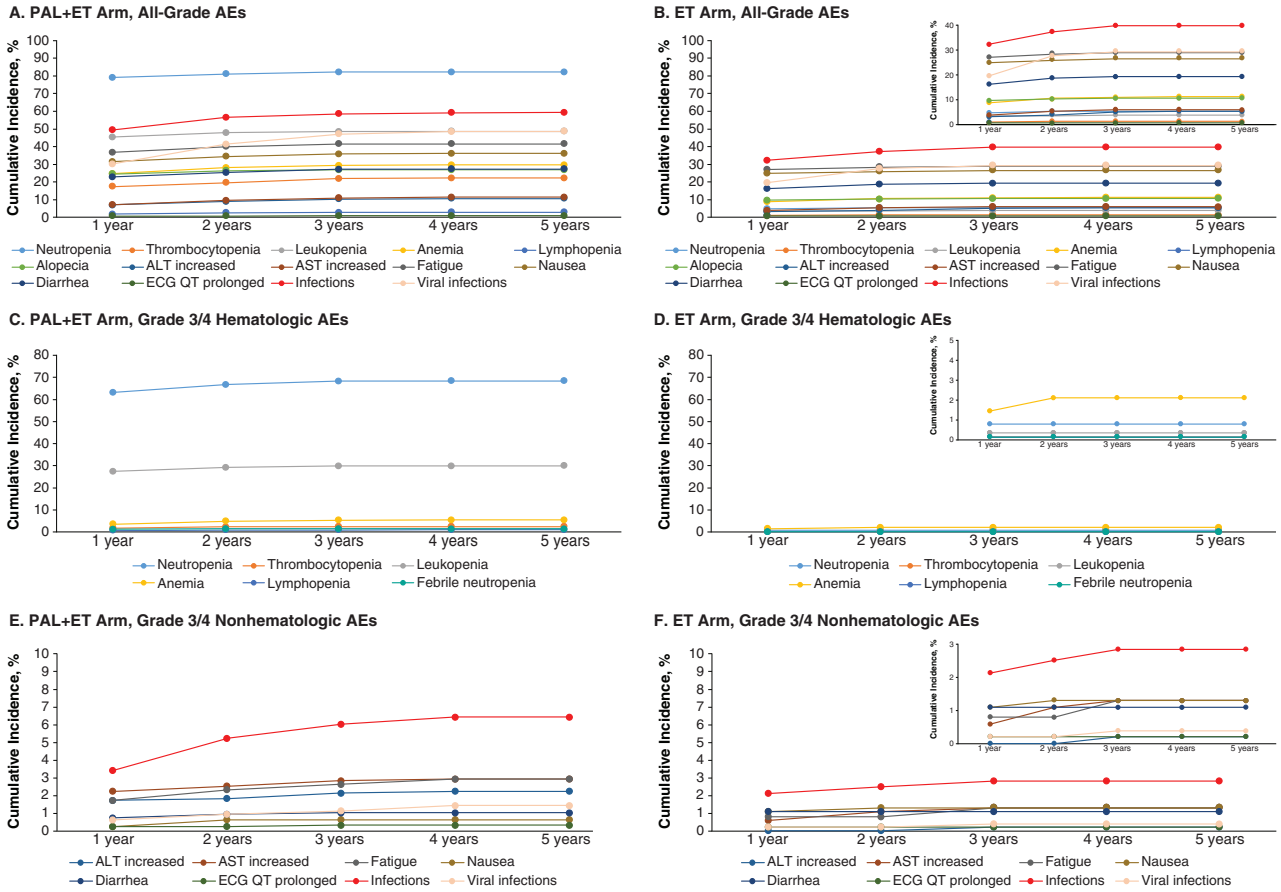

Figure 2. Cumulative incidence of selected AEs for patients in the palbociclib plus ET (n = 872) or ET (n = 471) groups[a,b]. **(A):** PAL + ET arm, all-grade AEs. **(B):** ET arm, all-grade AEs. **(C):** PAL + ET arm, grade 3/4 hematologic AEs. **(D):** ET arm, grade 3/4 hematologic AEs. **(E):** PAL + ET arm, grade 3/4 nonhematologic AEs. **(F):** ET arm, grade 3/4 nonhematologic AEs.
[a]Cumulative incidence is based on total number of patients included within each treatment arm for the full study period.
[b]Number of patients still on treatment at years 1, 2, 3, 4, and 5 were 510 (58.5%), 316 (36.2%), 192 (22.0%), 15 (1.7%), and 6 (0.7%), respectively, for palbociclib plus ET and 188 (39.9%), 95 (20.2%), 48 (10.2%), 4 (0.8%), and 2 (0.4%) for ET.
Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECG, electrocardiogram; ET, endocrine therapy; PAL, palbociclib.

grade 3; ILD was reported in a total of three patients in the ET group (supplemental online Table 1). The incidence of ILD did not appear to differ by geographic location in either treatment arm. The mean and median times to onset of ILD were 647.8 and 421.0 days, respectively, in the palbociclib plus ET group and 447.3 and 449.0 days in the ET group. Among patients receiving palbociclib plus ET with reported ILD, the mean age was 62 years and the median age was 65 years; 3 of the 13 cases were considered an SAE, and at the data cutoff date, six cases had resolved. No fatal cases of ILD were reported. After adjusting for treatment exposure, the incidence rate of ILD per person-year was 0.0085 with palbociclib plus ET and 0.0069 with ET.

Discussion

This updated analysis based on data pooled from the three PALOMA studies is the largest and longest-term analysis of the safety of a CDK4/6 inhibitor in combination with ET to date for the treatment of advanced breast cancer. This analysis, including data up to the first 5 years of treatment, included 872 patients who received palbociclib plus ET and 471 who received ET. Overall, the safety profile of palbociclib plus ET is consistent with findings from the previous long-term pooled safety analysis of palbociclib plus ET, without evidence for cumulative toxicity [17]. Both hematologic and nonhematologic AEs were reported in the initial months of treatment, and the cumulative incidence did not increase out to 5 years. The most common AEs associated with palbociclib were hematologic, specifically neutropenia.

Neutropenia is a known, common, and potentially serious AE associated with palbociclib and all CDK4/6 inhibitors [1, 18, 19]. However, dose reductions, dosing interruptions, or cycle delays of palbociclib have been shown to effectively manage neutropenia without compromising the benefits of palbociclib plus ET combination therapy [20–22]. Findings from a recent analysis of data pooled from the three PALOMA studies showed that reducing palbociclib dose decreased the frequency and severity of neutropenia regardless of patients' ethnicity, body mass index, or age [20]. Importantly, a landmark analysis of data from PALOMA-2 demonstrated that PFS in patients receiving palbociclib plus letrozole was similar between those whose dose was reduced and those who did not have their dose

reduced [22]. Similarly, in PALOMA-3, no differences in PFS were observed in patients treated with palbociclib plus fulvestrant who had their dose reduced because of neutropenia compared with those who did not have their dose reduced [21].

Because of potential neutropenia from their cancer treatments and a weakened immune system from the disease, patients with cancer are generally at higher risk for infections [23], a particular concern during the present coronavirus disease 2019 (COVID-19) pandemic [24]. Recent breast cancer management and treatment recommendations for use in the COVID-19 era were issued by the European Society for Medical Oncology and note that the risk of neutropenia associated with CDK4/6 inhibitors and infections has not been clearly defined and that CDK4/6 inhibitor plus ET treatment is recommended based on ongoing guidelines, local practice, and availability of resources [25]. However, patients receiving a CDK4/6 inhibitor should be closely monitored for symptoms of infections [25]. In this analysis the hazard ratio was 1.6 (p = .0995) for grade 3/4 infections and 1.8 (p = .4358) for grade 3/4 viral infections in the palbociclib plus ET group compared with the ET group. The overlapping of viral infections (all grades) and grade 3/4 neutropenia occurred in 63 (10.5%) patients in the palbociclib plus ET group, with the majority (99.8%) of viral infections being grade 1/2 in severity. Overlapping grade 3/4 viral infections occurred in only one (0.2%) patient with grade 3/4 neutropenia. In addition, the incidence of febrile neutropenia was low (1.4% of patients in the palbociclib plus ET group). Our findings suggest there is limited or no correlation between neutropenia and viral infections; however, patients who have additional risk factors that make them susceptible to infection (e.g., elderly, weakened immune systems) should be carefully monitored for signs of infection.

Interstitial lung disease and pneumonitis, which are potentially serious AEs associated with many other treatments for breast cancer [26], have recently been reported with CDK inhibitors, including palbociclib [1, 18, 19]. Findings from the current analysis showed that the incidence of ILD (0.23%) and pneumonitis (0.46%) was low with palbociclib plus ET. Although the incidence of ILD did not appear to differ by geographic region, these data are limited by the small sample size. No deaths from ILD occurred in the studies included in the current analysis, but fatal cases of ILD/pneumonitis have been reported in the postapproval setting [1]. It is challenging, however, to determine causality in the *real-world* environment. In both the clinical study and the postapproval setting, deaths from ILD/pneumonitis have also been reported for ribociclib and abemaciclib [18, 19].

A limitation of this analysis is that the findings might not be generalizable to the overall population of patients with ABC, as patients who met the inclusion and exclusion criteria for the PALOMA studies may not be representative of real-world patients. Additionally, most patients (>75%) in this analysis were White. Moreover, no definitive predictive markers for short- or long-term toxicity were discovered to help identify patients who may better tolerate palbociclib combination therapy. Strengths of this updated analysis include the large number of patients with long exposure to treatment pooled from the three PALOMA studies. This analysis represents almost 2,000 patient-years of treatment exposure, with 73% representing palbociclib plus ET treatment, and included AEs reported for 872 patients in the palbociclib plus ET arm.

Conclusion

This 5-year analysis demonstrates that palbociclib plus ET has a consistent and stable safety profile without cumulative or delayed toxicities. These findings further support palbociclib plus ET as an effective, safe, and manageable treatment for patients with HR+/HER2− ABC.

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Data Availability Statement

Upon request, and subject to certain criteria, conditions, and exceptions (see https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information), Pfizer will provide access to individual deidentified participant data from Pfizer-sponsored global interventional clinical studies conducted for medicines, vaccines, and medical devices (a) for indications that have been approved in the United States and/or European Union or (b) in programs that have been terminated (i.e., development for all indications has been discontinued). Pfizer will also consider requests for the protocol, data dictionary, and statistical analysis plan. Data may be requested from Pfizer trials 24 months after study completion. The deidentified participant data will be made available to researchers whose proposals meet the research criteria and other conditions, and for which an exception does not apply, via a secure portal. To gain access, data requestors must enter into a data access agreement with Pfizer.

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Disclosures

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