# Abstract

The study used the Flatiron Health Analytic Database to compare the overall survival (OS) in patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) metastatic breast cancer (MBC) who were treated with first-line palbociclib plus an aromatase inhibitor versus an aromatase inhibitor alone in routine US clinical practice. The study included 2888 patients who initiated treatment between February 3, 2015 and March 31, 2020, with at least 6 months of follow-up. After adjusting for various factors, the study found that the median OS was significantly longer in the palbociclib group compared to the aromatase inhibitor group. The real-world progression-free survival was also longer in the palbociclib group. These findings support the use of first-line palbociclib plus an aromatase inhibitor treatment in patients with HR+/HER2- MBC. It is important to note that the study was funded by Pfizer Inc, the manufacturer of palbociclib.

The results showed that patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer treated with first-line palbociclib plus an aromatase inhibitor had significantly longer overall survival and progression-free survival compared to those treated with an aromatase inhibitor alone.

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# Background

Oncologists, healthcare professionals, and researchers interested in the real-world effectiveness and safety of palbociclib plus an aromatase inhibitor for the treatment of hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer in postmenopausal women and men.

The study was carried out to evaluate the overall survival (OS) and real-world progression-free survival (rwPFS) of palbociclib, a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, in combination with an aromatase inhibitor versus an aromatase inhibitor alone in postmenopausal women and men with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2–) metastatic breast cancer (MBC) in routine clinical practice in the United States. The purpose of the study was to gather real-world evidence to validate the efficacy and safety of palbociclib in routine clinical practice and to assess its effectiveness compared to standard treatment options. Real-world studies are important as they allow for the inclusion of patients who may be underrepresented in clinical trials, making the findings more generalizable to patients treated in routine care. The study aimed to reinforce treatment recommendations and provide additional evidence on the safety and effectiveness of CDK4/6 inhibitors in the real-world setting. Previous real-world studies on palbociclib had limitations, such as a lack of a comparator group, small sample size, and short follow-up, and there was a need for more comprehensive research with longer-term follow-up. Therefore, this study was conducted to address these limitations and provide a more thorough evaluation of the OS and rwPFS outcomes of palbociclib in routine clinical practice.

Metastatic breast cancer refers to breast cancer that has spread from the original site in the breast to other distant tissues in the body. It is a more advanced stage of breast cancer and is characterized by the presence of cancer cells in areas outside of the breast, such as the bones, liver, lungs, or brain. The 5-year survival rate for metastatic breast cancer is relatively low, highlighting the need for effective treatment options for this condition.

HER2- breast cancer refers to breast cancer that does not have an overexpression or amplification of the human epidermal growth factor receptor 2 (HER2) gene. This subtype accounts for the majority of breast cancer cases and is typically hormone receptor-positive, meaning it responds to hormone therapies.

HR+ breast cancer refers to breast cancer that is hormone receptor-positive. This means that the cancer cells have receptors for hormones, specifically estrogen and/or progesterone. These receptors play a role in the growth and spread of the cancer, and targeting them with hormone therapy can be an effective treatment approach.

HR+/HER2- breast cancer refers to a subtype of breast cancer where the tumor cells have hormone receptors (HR+) for estrogen and/or progesterone, but do not have the human epidermal growth factor receptor 2 (HER2-) gene amplification.

Palbociclib is a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor that is used as a treatment for hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2–) metastatic breast cancer (MBC). It works by inhibiting the activity of CDK4/6 enzymes, which are involved in cell cycle progression. By blocking these enzymes, palbociclib helps to slow down tumor growth by preventing cancer cells from dividing and multiplying. This treatment is typically used in combination with endocrine therapy, such as an aromatase inhibitor, and has been shown to significantly prolong progression-free survival and overall survival in clinical trials and real-world studies.

An AI (aromatase inhibitor) is a type of hormone therapy used in the treatment of hormone receptor-positive breast cancer. It works by blocking the enzyme aromatase, which is responsible for converting androgens into estrogen, thereby reducing the levels of estrogen in the body.

Combining palbociclib, a CDK4/6 inhibitor, with an aromatase inhibitor (AI) is recommended as first-line treatment for HR+/HER2‒ MBC. This combination therapy has shown to significantly prolong median progression-free survival (PFS) and has demonstrated safety and effectiveness in real-world studies.

# Methods

This study was a retrospective analysis of electronic health records (EHRs) from the Flatiron Health Analysis Database. The database contains de-identified patient data from over 280 cancer clinics, representing more than 2.4 million actively treated US patients with cancer. The study included women aged 18 years or older with confirmed HR+/HER2- metastatic breast cancer (MBC) who received palbociclib plus an aromatase inhibitor or an aromatase inhibitor alone as first-line therapy for MBC between February 2015 and March 2020. The study had inclusion and exclusion criteria to select eligible patients. The primary outcome was overall survival (OS), and the secondary outcome was real-world progression-free survival (rwPFS). Statistical analyses were performed using different methods, including unadjusted analysis, stabilized inverse probability treatment weighting (sIPTW), and propensity score matching (PSM).

The study included women aged ≥18 years at MBC diagnosis with confirmed HR+/HER2‒ MBC at any point in patient history. They had a date of first prescription for palbociclib plus an aromatase inhibitor or an aromatase inhibitor alone as first-line therapy for MBC between February 3, 2015 and March 31, 2020.

# Results

The overall results of the study showed that patients who received palbociclib plus an aromatase inhibitor had a longer overall survival (OS) and progression-free survival (rwPFS) compared to those who received an aromatase inhibitor alone. The OS benefit was observed across most subgroups, regardless of race and presence of visceral or bone-only disease. The rwPFS benefit also varied by age subgroup, with patients aged ≥50 years having a greater benefit. Additionally, a significant proportion of patients in both groups received a CDK4/6 inhibitor as second-line treatment.

The results of this study indicate that the combination of palbociclib plus an aromatase inhibitor as first-line therapy for HR+/HER2‒ metastatic breast cancer (MBC) leads to improved overall survival (OS) and real-world progression-free survival (rwPFS) compared to treatment with an aromatase inhibitor alone. This benefit was observed across various subgroups, including different age groups and patients with or without visceral or bone-only disease. Additionally, the study found that a significant proportion of patients in both treatment groups received a CDK4/6 inhibitor as second-line treatment.

# Discussion

The key strengths of this study include the large sample size, diverse patient population, and longer follow-up time compared to previous analyses. The study used prespecified primary and secondary endpoints, as well as sensitivity analyses, to ensure robustness of the findings. The use of statistical methods such as sIPTW and PSM helped balance patient characteristics. The study also validated the OS and rwPFS endpoints using external data sources.

The limitations of this study include the retrospective nature of the database study, which may have missing or erroneous data entry. Some subgroups analyzed may have insufficient sample size to identify significant differences in outcomes. Treatment and patient selection bias cannot be excluded since therapy was provided in routine clinical practice. Disease progression was not based on standard criteria. While statistical methods were used to balance patient characteristics, unobserved variables cannot be fully addressed. The findings may not be generalizable to other patient populations not represented in the database.

The original article on which this summary is based is not provided in the given context.

Additional resources on breast cancer can be found through reputable sources such as the American Cancer Society, National Cancer Institute, BreastCancer.org, and the Susan G. Komen Foundation.

# Funding

Based on the provided context, the study was sponsored by Pfizer Inc, AstraZeneca, Foundation Medicine, and other organizations. However, it is important to note that a formal editorial review and fact check will be performed at a subsequent draft, and the specific details of the study, such as registration on a publicly accessible website, are not mentioned.