# Background

Breast cancer is a significant public health concern in the United States, with a high incidence rate and mortality rate. In 2021, it was estimated that there would be 281,550 new cases of female breast cancer diagnosed and 43,600 deaths. Among breast cancer cases, approximately 6% of them have spread to distant tissues, known as metastatic breast cancer (MBC). The 5-year survival rate for MBC is only 29.0%, highlighting the urgent need for effective treatment options.  
  
The majority of breast cancer cases are hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2-), accounting for 68% of cases. Treatment recommendations for patients with first-line HR+/HER2- MBC include the use of a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor in combination with endocrine therapy. This recommendation is based on the National Comprehensive Cancer Network treatment guidelines.  
  
One such CDK4/6 inhibitor is palbociclib, which was approved in February 2015 as a first-line treatment for HR+/HER2- MBC in combination with an aromatase inhibitor. It was later approved in February 2016 in combination with fulvestrant for patients who had progressed while on prior endocrine therapy. The efficacy of palbociclib was demonstrated in the phase 3 PALOMA-2 trial, where it was compared to letrozole plus placebo as a first-line treatment for estrogen receptor-positive/HER2- MBC. The trial showed that palbociclib plus letrozole significantly prolonged median progression-free survival (PFS) compared to letrozole plus placebo. However, overall survival (OS) data from the PALOMA-2 trial are not yet mature.  
  
Real-world evidence plays a crucial role in validating the efficacy and safety of drugs in routine clinical practice. It allows for the inclusion of patients who may be underrepresented in clinical trials and helps reinforce treatment recommendations. In the case of palbociclib, emerging real-world data have demonstrated its safety and effectiveness when used in combination with endocrine therapy for HR+/HER2- MBC.  
  
Two real-world studies conducted using the Flatiron Health Analytic Database showed positive results for palbociclib. The first study, a comparative effectiveness analysis, demonstrated longer real-world progression-free survival (rwPFS) and overall survival (OS) among patients treated with palbociclib plus letrozole compared to letrozole alone. The second study also showed a higher chance of tumor response with palbociclib plus letrozole and a significant improvement in median rwPFS and OS with combination therapy. However, both studies had limitations, including small sample sizes and short follow-up times, particularly for OS.  
  
Given the importance of real-world evidence and the need for more robust data on the effectiveness of palbociclib in routine clinical practice, the purpose of this study was to evaluate OS and rwPFS of palbociclib plus aromatase inhibitor (AI) versus AI alone in postmenopausal women and men with HR+/HER2- MBC. This study utilized the Flatiron Health Analytic Database, which provides a large and diverse patient population, allowing for a more comprehensive analysis. Importantly, this study has the longest index period from palbociclib approval, spanning 7 years, and includes an extended follow-up time of at least 6 months from the index date to the data cutoff date.  
  
By conducting this study, the authors aim to address the existing gap in real-world evidence for palbociclib and provide valuable insights into its effectiveness and safety in routine clinical practice. The findings of this study will contribute to the growing body of evidence on the use of palbociclib in HR+/HER2- MBC and help guide treatment decisions for healthcare providers. Ultimately, the goal is to improve patient outcomes and survival rates for individuals with HR+/HER2- MBC.