# Background

Breast cancer is a significant public health concern in the United States, with a high incidence and mortality rate. In 2021, it was estimated that there would be 281,550 new cases of female breast cancer and 43,600 deaths. Among breast cancer cases, approximately 6% are classified as metastatic breast cancer (MBC), where the cancer has spread to distant tissues. 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. For patients with first-line HR+/HER2- MBC, the National Comprehensive Cancer Network treatment guidelines recommend the use of a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor in combination with endocrine therapy. This treatment approach has shown promising results in clinical trials and has become the standard of care for these patients.  
  
One such CDK4/6 inhibitor is palbociclib, which was approved in 2015 for the first-line treatment of HR+/HER2- MBC in combination with an aromatase inhibitor. In the phase 3 PALOMA-2 trial, palbociclib plus letrozole was compared to letrozole plus placebo as first-line treatment for estrogen receptor-positive/HER2- MBC. The trial demonstrated a significant prolongation of median progression-free survival (PFS) in patients receiving palbociclib plus letrozole. However, overall survival (OS) data from the 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. Emerging real-world data on palbociclib have demonstrated its safety and effectiveness in combination with endocrine therapy for HR+/HER2- MBC.  
  
Two comparative effectiveness studies using the Flatiron Health Analytic Database showed longer real-world PFS and OS among patients treated with palbociclib plus letrozole compared to letrozole alone. These studies also demonstrated a higher chance of tumor response with combination therapy. However, the real-world data on OS are limited by small sample sizes and short follow-up time.  
  
The purpose of this study is to further evaluate the OS and real-world PFS of palbociclib plus aromatase inhibitor (AI) versus AI alone in postmenopausal women and men with HR+/HER2- MBC in routine clinical practice in the United States. This study is significant because it uses the Flatiron Health Analytic Database, which provides a large and diverse patient population, allowing for more robust and generalizable results. Additionally, this study has the longest index period from palbociclib approval and includes an extended follow-up time of at least 6 months, providing valuable insights into the long-term outcomes of palbociclib treatment.  
  
In conclusion, breast cancer remains a significant health burden in the United States, and there is a need for effective treatment options, particularly for patients with HR+/HER2- MBC. Palbociclib, a CDK4/6 inhibitor, has shown promising results in clinical trials and real-world studies. This study aims to further evaluate the efficacy and safety of palbociclib plus AI in routine clinical practice, providing valuable insights into the long-term outcomes of this treatment approach.