# 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, 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%. 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.  
  
The National Comprehensive Cancer Network (NCCN) treatment guidelines recommend the use of a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor in combination with endocrine therapy as the first-line treatment for pre- and postmenopausal women, as well as men, with HR+/HER2- MBC. One such CDK4/6 inhibitor is palbociclib, which was approved in February 2015 for use in combination with an aromatase inhibitor as first-line treatment for HR+/HER2- MBC. It was later approved in February 2016 for use in combination with fulvestrant for patients who had progressed while on prior endocrine therapy.  
  
The PALOMA-2 trial, a phase 3 clinical trial, evaluated the efficacy of palbociclib plus letrozole compared to letrozole plus placebo as first-line treatment for estrogen receptor-positive/HER2- MBC. The trial demonstrated that the combination of palbociclib and letrozole significantly prolonged median progression-free survival (PFS) in these patients. 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. Real-world studies provide an opportunity to include patients who are often underrepresented in clinical trials and help reinforce treatment recommendations. Emerging real-world data on palbociclib have demonstrated its safety and effectiveness when used in combination with endocrine therapy for HR+/HER2- MBC.  
  
Two comparative effectiveness real-world studies using the Flatiron Health Analytic Database showed that palbociclib plus letrozole resulted in longer real-world progression-free survival (rwPFS) and overall survival (OS) compared to letrozole alone. Another study in the same database found that the combination therapy increased the chance of tumor response and significantly improved median rwPFS and OS. However, these studies were limited by small sample sizes and short follow-up times, particularly in terms of OS.  
  
The purpose of the current study is to address the existing gap in real-world evidence by evaluating the OS and rwPFS 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 unique in that it has the longest index period from palbociclib approval, as the drug has been available for the treatment of HR+/HER2- MBC for 7 years. Additionally, the study 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 provide further evidence on the effectiveness and safety of palbociclib plus AI in real-world clinical practice. The findings of this study will contribute to the existing body of knowledge on the treatment of HR+/HER2- MBC and help guide clinical decision-making. The study's results will also have implications for treatment guidelines and may potentially lead to improved outcomes for patients with HR+/HER2- MBC.  
  
In conclusion, breast cancer is a significant health issue in the United States, and the majority of cases are HR+/HER2-. The NCCN recommends the use of a CDK4/6 inhibitor in combination with endocrine therapy as the first-line treatment for HR+/HER2- MBC. Palbociclib is one such CDK4/6 inhibitor that has shown promising results in clinical trials. Real-world evidence has further supported the efficacy and safety of palbociclib plus endocrine therapy. However, there is a need for more robust real-world data, particularly in terms of OS. The current study aims to address this gap by evaluating the OS and rwPFS of palbociclib plus AI versus AI alone in routine clinical practice. The findings of this study will contribute to the understanding of the optimal treatment approach for HR+/HER2- MBC and may have implications for clinical practice and patient outcomes.