# 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. 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 and applies to both pre- and postmenopausal women, as well as men with HR+/HER2- MBC.  
  
One such CDK4/6 inhibitor is palbociclib, which was approved in 2015 as a first-line treatment for HR+/HER2- MBC in combination with an aromatase inhibitor. In 2016, it was also approved 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 significantly prolonged median progression-free survival (PFS) when used in combination with letrozole 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. 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. These studies also demonstrated a higher chance of tumor response with