# 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 (NCCN) 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 improving outcomes for both 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 the first-line treatment of 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 PALOMA-2 trial, a phase 3 study, evaluated the efficacy of palbociclib plus letrozole versus 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) with the combination therapy, although overall survival (OS) data 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. Comparative effectiveness studies using the Flatiron Health Analytic Database have shown longer real-world PFS and OS among patients treated with palbociclib plus letrozole compared to letrozole alone. These studies also