# 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 these cases, approximately 6% of breast cancers have spread to distant tissues, known as metastatic breast cancer (MBC), which is associated with a 5-year survival rate of 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 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. 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 was associated with longer real-world progression-free survival (rwPFS) and overall survival (OS) compared to letrozole alone.