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# CLEE011AUS74 Study Results Abstract for Public Disclosure

**Title**

Real World Treatment Patterns and Outcomes in HR+, HER2- Metastatic Breast Cancer Patients Treated with CDK 4/6 Inhibition in the First Line (1L) Setting

**Keywords**

Ribociclib, CDK4/6i, metastatic breast cancer

**Rationale and background**

Breast cancer is the second most common cancer among women in the United States (US) and it is estimated that 310,720 new cases will be diagnosed in 2024.[1] About 60% of patients present with localized disease, 30% with regional disease and 6% with distant disease. Unfortunately, about 30% of patients diagnosed with early-stage disease will eventually develop metastatic disease.[2] Hormone receptor–positive (HR+), human epidermal growth factor receptor-2–negative (HER2–) is the most common subtype, accounting for about 80% of all breast cancer cases.[3] Patients diagnosed with metastatic breast cancer (mBC) have a poor prognosis with the 5-year survival rate being 30%.[1,4] In this setting, cyclin dependent kinase 4/6 inhibitors (CDK4/6i), ribociclib, palbociclib and abemaciclib, have been shown to offer substantial clinical benefits to HR+/HER2- patients. Ribociclib + endocrine therapy (ET) is recommended by the National Comprehensive Cancer Network® (NCCN) as NCCN category 1 preferred CDK4/6i for first-line (1L) treatment of HR+/HER2- mBC with no visceral crisis in postmenopausal patients or premenopausal patients with ovarian ablation/suppression[5]. In addition to overall survival and progression-free survival benefits, 1L ribociclib + ET demonstrated a tolerable and manageable safety profile across all phase 3 MONALEESA (MONALEESA-2,-3,-7) randomized controlled trials (RCTs)[6]. There is limited real-world data allowing for examination of the utilization and outcomes of the different CDK4/6i treatments in mBC. As such, this pilot study aims to further elucidate, among HR+/HER2- mBC patients, these real-world CDK4/6i treatment patterns and outcomes.

**Research question and objectives**

Primary Objective: Describe patient profiles, baseline demographics, clinical characteristics including comorbidities, and treatment patterns among patients with HR+/HER2- mBC treated with 1L ribociclib in a real-world setting

Secondary Objective: Describe ribociclib dosing patterns, including starting doses, dose adjustments (including temporary dose holds if available), among patients with HR+/HER2- mBC treated with 1L ribociclib in a real-world setting

**Study design**

An observational real world retrospective study was conducted, utilizing data derived from deidentified electronic health records (secondary data use).

**Setting**

This study is designed as a retrospective cohort study that utilizes electronic health records from community oncology-based patient records in the US. The study population includes adult patients with HR+/HER2- metastatic breast cancer.

**Subjects and study size**

The study sample consisted of 480 patients obtained via stratified random sampling, for whom data were enriched by manual curation using an electronic case report form (eCRF). Since this is a descriptive study, a power/sample size calculation was not conducted. Patients were required to have HR+/HER2- mBC, were treated with first line ribociclib, palbociclib, or abemaciclib between April 1, 2017 and April 1, 2024, were female and age 18 or older, with a minimum of two visits up to and including mBC 1L treatment start. Patients were excluded if they received prior CDK4/6i therapy, prior 1L therapy in the metastatic setting, were diagnosed with another primary cancer other than breast cancer, or participated in a clinical trial.

**Variables and data sources**

Variables included demographics, clinical and disease characteristics, treatment characteristics, dosing characteristics, medical events, and clinical outcomes. The data source contains a harmonized dataset including electronic health data from structured and unstructured fields from community oncology practices. The data are harmonized using data sources from the electronic medical record (EMR), practice management systems, the Centers for Medicare and Medicaid Services (CMS) claims, pharmacy claims, and manual data abstraction. These various data sources are linked to a unique Medical Record Number (MRN) so that data can be analyzed across various systems and practice sites – allowing for longitudinal patient insights where the database contains multiple sites of care for a single patient. The additional value of a harmonized data set is that unique patient level data can be analyzed in the EMR, which allows us to evaluate outcomes. The clinical data source from the EMR includes structured fields containing diagnosis codes, laboratory values, comorbidities, treatments (e.g., dose, duration) and unstructured fields comprised of physician notes fields, genomics information (via genetic testing report, pathology reports, lab reports), etc. It is well accepted that community oncology data sets are inherently incomplete, and the various EMR systems vary significantly on the data points included as structured data fields. Abstraction can enrich data and provide a more complete data source. The abstracted data were collected using an eCRF. Details on vital status and dates of death were obtained by tokenizing system. The data source includes over 3 million primarily community oncology-based patient records in the US.

**Statistical methods**

Categorical variables were reported as proportions and continuous variables as mean ± standard deviation or median (range, interquartile range [IQR]), as appropriate. Kaplan-Meier analyses were conducted for time-event outcomes including associated time of follow-up and employing censoring rules. Since this is a retrospective study, the data available from the electronic health record was utilized. No inferential analyses were planned for the comparisons of outcomes between different CDK4/6i agents.

**Results**

*Primary Objectives*

Patients treated with ribociclib (n=160) had a median age of 64 years at 1L initiation, with median time from mBC diagnosis to 1L initiation of 0.9 months. There were 70 patients (43.8%) who were diagnosed with de novo metastatic breast cancer, most patients had Eastern Cooperative Oncology Group (ECOG) scores of 0 or 1, 11.9% were premenopausal, 82.5% were white, and the most common comorbidity was diabetes without chronic complications (4.8%). Median follow-up from 1L initiation was 22.2 months. The most common baseline metastasis for ribociclib patients was bone (83.2%), with 43.9% of patients with bone-only metastasis. The most common combination therapy with ribociclib was letrozole (n=91, 56.9%), and at the time of data cut off, most patients did not have second-line (2L) therapy (n=104, 65.0%).

*Secondary Objectives*

Among ribociclib patients, most patients (80.6%) initiated ribociclib at the recommended 600 mg dose and the majority did not have a dose adjustment (65.6%). Among the 105 patients without a dose adjustment, the starting dose distribution was 600 mg (80%), 400 mg (8.6%), 200 mg (4.8%), and unknown (6.7%). Among patients with available information (n=147), the median relative dose intensity (RDI) was 100%.

## Discussion

The sample of ribociclib patients treated in the first line sampled for this analysis had a median age of 64 at both mBC diagnosis and 1L initiation. Our study population included both premenopausal (11.9%) and postmenopausal (88.1%) women. The population in the MONALEESA-2 trial[7], which included only postmenopausal women, had a median age of 62. 40.0% of our ribociclib study population had an ECOG score of 0, with 40.6% of patients initially diagnosed with stage IV metastatic breast cancer. In MONALEESA-2, 61.1% of ribociclib patients had an ECOG of 0, with 34.1% of ribociclib patients presenting with newly diagnosed advanced or metastatic disease.

Most ribociclib patients in our study received combination therapy with aromatase inhibitor (AI) therapy while 31% received fulvestrant. The TTD reported in the MONALEESA-3 trial was 15.8 months[8]. Most ribociclib patients in our study did not continue on to a subsequent therapy. In MONALEESA-3, 39.0% of ribociclib patients did not have a subsequent therapy. These differences could be due to limitations in follow-up information as the median follow-up time for ribociclib patients in our study was 22.2 months, and our follow-up time may have ended before patients initiated a next treatment. There is limited real-world evidence in US populations assessing treatment patterns of patients after discontinuing ribociclib, and more research is needed to support the findings from this current study. The proportion of patients who had a dose reduction in this study was 30.6% vs 53.9% reported in the MONALEESA-2 trial. This could be due to the different study designs between our study and the clinical trial's wherein 100% of trial patients started at the 600 mg dose compared with 80.6% in our study population.

## Conclusion

This real-world study included patients with HR+/HER2- mBC treated in 1L with a CDK4/6i in the real-world setting. We found a lower proportion of patients initiating at the recommended ribociclib dose than what has been previously reported and a lower proportion of patients with a ribociclib dose reduction than what was reported in the clinical trial. Most patients in the clinical trials received therapy after discontinuing ribociclib, while most patients in our population did not receive 2L therapy, which may be due to limited follow up time in the study. More real-world research is needed, with longer follow-up, to verify these treatment and dosing patterns.

## References

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