Real World Rate of Switching and Reasons for Switching Among CDK4/6i Drugs Among First-Line Metastatic HR+/HER2- Breast Cancer Patients

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Background

- The combination of CDK4/6 inhibitor (CDK4/6i) (abemaciclib [abema], palbociclib [palbo], or ribociclib [ribo]) and endocrine therapy (ET) is standard-of-care for patients with hormone receptor-positive, HER2-negative metastatic breast cancer (HR+/HER2- mBC).
- These agents demonstrate similar improvements in progression-free-survival, but only ribo has shown consistent overall survival (OS) benefit across multiple phase III trials[1-3]. This clinical benefit, as well as toxicity profiles, comorbid conditions, physician familiarity, and patient-specific factors, may influence initial selection and switching patterns in clinical practice.
- This study characterizes switching patterns in patients initiating first-line (1L) CDK4/6i + ET.

Methods

- This retrospective cohort study included patients with HR+/HER2- mBC who initiated 1L treatment with abema, palbo, or ribo between 02/26/2018 and 05/16/2025.
- The study utilized Integra PrecisionQ de-identified electronic health record (EHR) database, which includes data on >3 million cancer patients treated across >500 US care sites.
- Switching was defined as discontinuation of the initial CDK4/6i followed by initiation of another CDK4/6i. Data on whether the accompanying ET was changed at the time of the CDK4/6i switch were not assessed.
- Patients (n=179) were selected for a subset analysis based on the availability of curated discontinuation reasons (toxicity, disease progression, personal/financial), which were manually abstracted from clinical documentation.
- Patients were stratified by initial CDK4/6i, documented reason for switching, and time to switch (≤30, 31–90, 91–180, >180 days). Differences in time to switch by reason were assessed using Wilcoxon rank-sum testing.

Results

Among 11,928 patients with HR+/HER2- mBC who initiated 1L treatment with CDK4/6i + ET, 7499 used palbo, 2371 used ribo, and 2058 used abema. Of these patients, 577 patients (7.7%) switched from palbo, 307 (12.9%) from ribo, and 264 (12.8%) from abema to an alternative CDK4/6i (Figure 1).

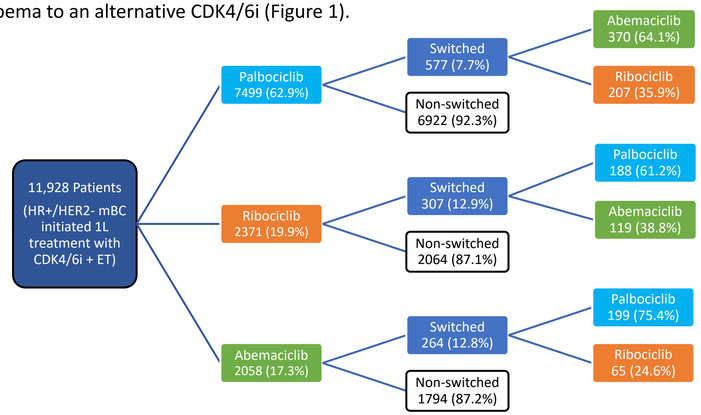


Figure 1. Switching Distribution for Patients With HR+/HER2- mBC Who Initiated 1L Treatment With CDK4/6i + ET

Switching Reasons And Duration of Therapy

- Toxicity was the most frequently documented reason for switching, reported in 91.8% of patients who switched from abema, 49.5% from palbo, and 69.7% from ribo (Figure 2).
- The median duration of therapy prior to switching for toxicity was longest for palbo (131 days), followed by abema (96 days) and ribo (95 days).
- Disease progression as a reason for switching was most commonly reported in patients initially treated with palbo (42.3%), followed by ribo (21.2%) and abema (6.1%) (Figure 2).
- Patients who switched due to disease progression had a significantly longer time to switch than those who switched for other reasons (median 444 vs. 141 days; Wilcoxon P<0.0001).

Results

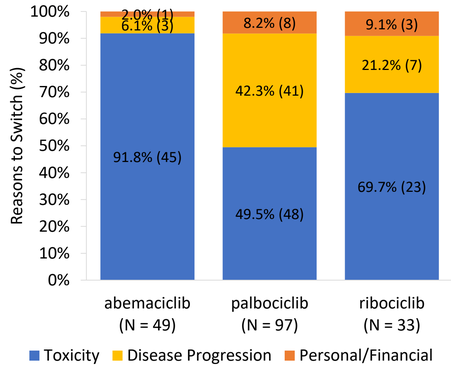


Figure 2. Reasons for Switches During 1L CDK4/6i Treatment

Switching Days

- Switches occurred most commonly after >180 days for palbo (58.8%), whereas earlier switches (≤180 days) were more frequent for abema and ribo (~70%) (Figure 3).

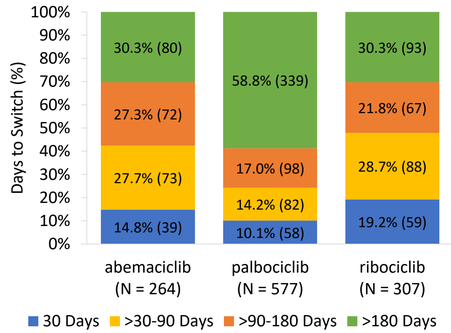


Figure 3. Days to Switches During 1L CDK4/6i Treatment

Results

- Among those who switched from palbo, 64.1% switched to abema and 35.9% to ribo (Figure 1).
- Among patients who switched from ribo, 61.2% switched to palbo and 38.8% to abema.
- Of those switching from abema, 75.4% switched to palbo and 24.6% to ribo.
- Baseline demographics were comparable across patient groups (data not shown).

Conclusions

- In this real-world analysis of 1L CDK4/6i use in HR+/HER2- mBC, intraclass switching was common and most often driven by toxicity rather than disease progression.
- Time to switch varied by initial agent and reason for discontinuation, with palbo users more frequently switching later and for progression, while earlier switches from abema and ribo were largely due to intolerance.
- This study's retrospective design may introduce selection bias, and reasons for switching were not always documented. Comorbidities, tumor burden, prior treatments, and access to care were not captured, representing potential unmeasured confounders.
- Additionally, evolving data availability and drug approvals during the study period may have influenced treatment choices and switching patterns.

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