Treatment Outcomes of Patients with Early-Stage Breast Cancer Eligible, but Not Treated, with Adjuvant Ribociclib. A Real-World Cohort Study

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Abstract

- Adjuvant cyclin-dependent kinase (CDK) 4/6 inhibitors, such as ribociclib and abemaciclib, have demonstrated significant disease-free survival (DFS) benefits in early-stage hormone receptor-positive (HR+)/HER2-negative breast cancer within randomized trials[1,2].
- However, real-world implementation remains limited, and outcomes for eligible-but-untreated populations are poorly characterized. This study evaluates treatment outcomes in patients retrospectively classified as eligible for adjuvant CDK4/6 inhibition under NATALEE criteria, all of whom were managed without such agents in routine practice.

Introduction

- Endocrine therapy, typically with tamoxifen or aromatase inhibitors (AI), has long served as the cornerstone of adjuvant treatment for HR+/HER2- breast cancer[3].
- The NATALEE trial, a multicenter, randomized, phase III study, assessed the efficacy of ribociclib combined with nonsteroidal AI in patients with high-risk HR-positive/HER2-negative early breast cancer[1].
- This trial analysis revealed a statistically significant reduction in risk of invasive disease recurrence or death, with 3-year iDFS rates of approximately 90.7% for the ribociclib combination group versus 87.6% with endocrine therapy alone[1].
- In this study, we performed a retrospective cohort analysis of early-stage HR-positive/HER2-negative breast cancer patients, retrospectively applying NATALEE eligibility criteria, and assessed survival outcomes in these CDK4/6i-eligible patients who did *not* receive CDK4/6 inhibitors.

Methods and Materials

- This study was a retrospective cohort analysis of patients with early-stage HR-positive/HER2-negative breast cancer treated at our institution between January 2005 and December 2020.
- Eligible patients were identified from a prospectively maintained institutional breast cancer database. All data was retrieved from electronic medical records.
- All 2,730 patients included were aged ≥18 years at diagnosis with histologically confirmed invasive breast carcinoma, HR+ (estrogen receptor [ER] and/or progesterone receptor [PR] expression ≥1% by immunohistochemistry (IHC) and HER2-negative disease (IHC) 0–1+, or 2+ with non-amplified FISH).
- All patients underwent curative-intent surgical resection and received standard-of-care adjuvant endocrine therapy with or without chemotherapy.
- Patients with stage IV disease, HER2-positive tumors, HR-negative or missing receptor status, were excluded.

Table 1: Patients Characteristics

Characteristics	N(%)	Characteristics	N(%)
Gender		**cT**	
Female	2700 (98.9%)	**cT1**	581 (21.3%)
Male	30 (1.1%)	**cT2**	1314 (48.1%)
Age group at diagnosis		**cT3**	460 (16.8%)
>50	1313 (48.1%)	**cT4**	142 (5.2%)
≤50	1417 (51.9%)	**cTx**	233 (8.5%)
Histology		**cN**	
IDC	2213 (81.1%)	**cN+**	1208 (44.2%)
ILC	280 (10.3%)	**cN0**	1300 (47.6%)
Other	237 (8.7%)	**cNx**	222 (8.1%)
Estrogen-receptors		**Neoadjuvant chemotherapy**	
Negative	91 (3.3%)	**No**	1687 (61.8%)
Positive	2618 (95.9%)	**Yes**	1043 (38.2%)
Grade		**Adjuvant Chemotherapy**	
1	373 (13.7%)	**No**	1657 (60.7%)
2	1509 (55.3%)	**Yes**	1069 (39.2%)
3	741 (27.1%)		

Results

- Perioperative chemotherapy was administered to 2505 patients (91.7%). None of the patients received CDK4/6i. Endocrine therapy was given to nearly all patients (99.1%), with AI prescribed in 1,422 patients (52.1%) and tamoxifen in 1,035 patients (37.9%).
- A total of 1,955 patients (71.6%) met the trial-defined criteria for adjuvant ribociclib. Median follow-up was 63 months.
- The 3-year DFS was 85.2% (95% CI: 83.6%-86.8%) in the eligible group compared to 95.1 (95% CI: 93.5%-96.6%) in the ineligible group with a highly significant p-value < 0.0001).
- The estimated 5-year OS in the eligible group was 87.9% (95% CI: 86.4%-89.5%) compared to 95.9% (95% CI: 94.4%-97.4%) in the ineligible group with a highly significant p-value < 0.0001). The majority of deaths in the eligible cohort were attributed to distant metastatic relapse.

Discussion

- The findings of our study provide valuable real-world benchmark of outcomes in the absence of adjuvant CDK4/6 inhibition. In practice, this can inform shared decision-making by applying trial data within everyday oncology practice.
- These findings are consistent with the known prognostic burden of high-risk features in HR-positive/HER2-negative disease, including larger tumor size, nodal involvement, high histologic grade, and lower ER expression levels.
- Our eligible population showed an expected worse outcomes. These data illustrates the higher recurrence risk among those meeting ribociclib eligibility criteria and emphasize the potential benefit that may have been realized had CDK4/6i therapy been administered.

Figure 1. 3-year and 5-year DFS

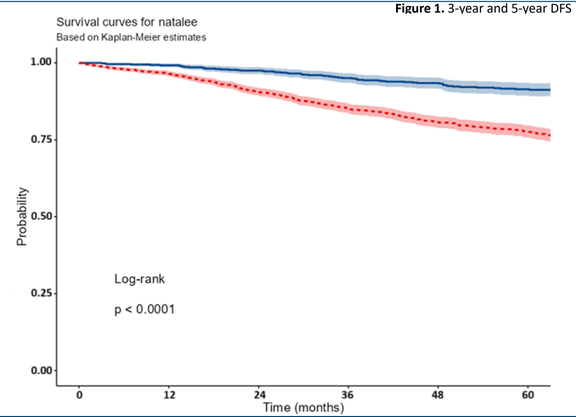
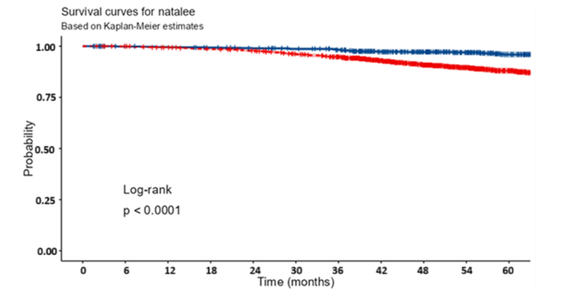


Figure 2. 5-year OS



Conclusions

- These findings mirror the risk stratification observed in clinical trials and highlight the real-world impact of failing to implement CDK4/6i therapy in high-risk early-stage breast cancer. Bridging the gap between evidence and practice is crucial to improving treatment outcomes in this group of patients.

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