



# Efficacy of Palbociclib and Ribociclib in Second-line Treatment of Metastatic Hormone Receptor-positive Breast Cancer: A Single-center Experience

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## ABSTRACT

**Objective:** Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors represent the standard of care for the first-line treatment for hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer. Increasing evidence suggests that CDK4/6 inhibitors may also be a viable option in second-line treatment. This study aimed to compare the efficacy of palbociclib and ribociclib in second-line treatment for HR+ HER2-negative metastatic breast cancer patients and to identify factors influencing treatment response.

**Material and Methods:** We retrospectively analysed 112 patients who received either palbociclib (n=52) or ribociclib (n=60) as second-line treatment between January 2018 and December 2023 at our hospital. We evaluated demographic characteristics, clinical and pathological data, overall survival (OS), and progression-free survival (PFS), alongside factors potentially affecting these outcomes, including age, Eastern Cooperative Oncology Group (ECOG) performance status, metastasis pattern, and endocrine resistance.

**Results:** Median PFS was 16.1 months for the palbociclib group and 20.3 months for the ribociclib group (p=0.214), while median OS was 38.1 months and 37.5 months, respectively (p=0.308). Multivariate analysis identified ECOG performance status as an independent prognostic factor (hazard ratio: 1.86, 95% confidence interval: 1.18-2.94, p=0.028). Longer PFS was observed in patients who were endocrine-sensitive or those receiving hormone therapy (25.2 months for endocrine-sensitive patients and 27.3 months after hormone therapy).

**Conclusion:** In terms of treatment efficacy in second-line therapy, palbociclib and ribociclib are comparable. Treatment response was predominantly influenced by the patient's performance status. These findings may guide clinicians in making treatment decisions based on individual patient characteristics.

**Keywords:** CDK4/6 inhibitors; metastatic breast cancer; palbociclib; ribociclib; progression-free survival

## INTRODUCTION

Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors have marked a significant milestone in the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer (MBC). These drugs inhibit the proliferation of cancer cells by targeting enzymes essential for cell division.<sup>1</sup> Currently, the combination of

CDK4/6 inhibitors and aromatase inhibitors is considered the standard first-line treatment for HR+/HER2- advanced/MBC.<sup>2</sup> Large-scale Phase III studies have demonstrated that the addition of CDK4/6 inhibitors to endocrine therapy significantly improves progression-free survival (PFS) in both first- and second-line treatments.<sup>1,3,4</sup> Despite their high toxicity profile and cost, CDK4/6 inhibitors are recommended for first-line use.<sup>5</sup> However, due to their cost, the requirement for

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regular monitoring, and their toxicity profile, some clinicians opt to delay their use until second-line therapy.<sup>1</sup>

The recently published SONIA study is noteworthy as the first randomized trial to compare the first- and second-line use of CDK4/6 inhibitors in HR+/HER2- advanced breast cancer. The results of this study showed no statistically significant benefit for first-line use of CDK4/6 inhibitors compared to their use in the second-line setting.<sup>6</sup>

Currently, prospective studies comparing the efficacy of CDK4/6 inhibitors in first- and second-line treatments remain limited.<sup>7</sup> Specifically, no randomized controlled trials have directly compared the efficacy and safety of palbociclib and ribociclib.<sup>8</sup> Furthermore, the mechanisms underlying resistance to CDK4/6 inhibitors have yet to be fully elucidated, and the optimal treatment strategy for patients who develop resistance to these drugs remains undetermined.<sup>9</sup> Real-life studies complement randomized controlled trials and provide valuable evidence that may help address unresolved clinical questions.<sup>7</sup>

In this context, we aimed to compare the efficacy and safety of palbociclib and ribociclib when used as second-line treatments for HR+/HER2- MBC patients in our centre.

## MATERIAL AND METHODS

### Study Design and Patient Selection

This single center retrospective observational study analysed the medical records of patients treated with CDK4/6 inhibitors (palbociclib or ribociclib) as second-line therapy for HR+ HER2-negative MBC between January 2018 and December 2023. The choice of which CDK4/6 inhibitor to use was based on physician preference according to patients' age, general condition, drug availability, and comorbidities. Inclusion criteria included a histopathologically confirmed diagnosis of HR+ [estrogen receptor (ER)  $\geq 10\%$ ], HER2-negative MBC, treatment with palbociclib or ribociclib in the second-line setting, and availability of regular follow-up data. Patients who received CDK4/6 inhibitors in first-line treatment were younger than 18 years, or lacked sufficient follow-up data were excluded.

### Data Collection and Evaluation

Demographic, clinical, and pathological data were retrieved from hospital electronic records. The following variables were recorded: age, menopausal status, Eastern Cooperative Oncology Group (ECOG) performance status, histological subtype, tumour biomarkers ER, progesterone receptor, Ki-67, metastasis patterns (localization, number), prior treatments, and treatment response. Endocrine resistance was categorized as follows: *de novo* metastatic patients and those who experienced recurrence greater than 12 months after

adjuvant endocrine therapy were classified as endocrine-sensitive within a broader resistance classification framework. Patients with recurrence  $\leq 12$  months after adjuvant therapy or progression within 12 months after first-line endocrine therapy were classified as endocrine-resistant. PFS and overall survival (OS) were assessed in both treatment groups.

### Statistical Analysis

SPSS version 28.0 was used for statistical analysis. Descriptive statistics, including means, standard deviations, medians, and ranges for continuous variables, and frequencies and percentages for categorical variables, were computed. The normality of data distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Comparisons between continuous variables with normal distribution were performed using the Independent Samples t-test, while the Mann-Whitney U test was applied to non-normally distributed variables. Chi-square tests were used for categorical variables. Survival analyses were performed using the Kaplan-Meier method, with differences assessed by log-rank tests. Cox regression analysis was conducted to identify prognostic factors. A p-value of  $<0.05$  was considered statistically significant.

### Ethical Considerations

The study was approved by the Ethics Committee of University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital Scientific Research Ethics Board (decision no: 2025/010.99/12/25, date: 24.01.2025) and conducted in accordance with the principles outlined in the Declaration of Helsinki. Given the retrospective nature of the study, patient consent was not obtained; however, all data were processed and analysed in accordance with confidentiality protocols.

## RESULTS

The mean age of patients in the palbociclib group was  $59.8 \pm 12.9$  years (median: 60.5), and in the ribociclib group, was  $58.6 \pm 12.5$  years (median: 61.0). ER expression levels were high in the majority of patients, and only a small proportion ( $n=2$ , 1.7%) had low ER expression (1-10%). These two individuals had an ER expression of 10%. Palbociclib was used by one of these two patients, and ribociclib by the other. Four individuals (3.4%) had ER expression levels ranging from 11% to 40%. Similarly, two of the four patients received ribociclib, while the other two received palbociclib. ECOG performance status was as follows: 57.7% of patients in the palbociclib group had ECOG-0, 34.6% had ECOG-1, and 7.7% had ECOG-2, while in the ribociclib group, 73.3%, 21.7%, and 5.0% were classified as ECOG-0, ECOG-1, and ECOG-2, respectively. Menopausal status was similar between groups: 75% of patients in the palbociclib group were postmenopausal, and 66.7% in the ribociclib group were postmenopausal (Table 1).

Histologically, ductal carcinoma was the most common type in both groups (50% in the palbociclib group, 43.3% in the ribociclib group). Ki-67 proliferation indexes were  $27.2 \pm 16.2\%$  in the palbociclib group and  $28.0 \pm 18.6\%$  in the ribociclib group. No significant differences were observed between the groups in terms of demographic or clinical characteristics.

Regarding metastasis patterns, the rates of *de novo* metastatic disease were 50.0% in the palbociclib group and 55.0% in the ribociclib group. Liver metastasis occurred in 26.9% of the palbociclib group and 18.3% of the ribociclib group, while isolated bone metastasis was found in 36.5% and 26.7%, respectively. The rate of endocrine resistance was 23.1%

**TABLE 1: Demographic, clinical, disease characteristics, and survival analysis.**

Category	Parameter	Palbociclib (n=52)	Ribociclib (n=60)	p-value
Age (years)	Mean $\pm$ SD	59.8 $\pm$ 12.9	58.6 $\pm$ 12.5	0.616 <sup>t</sup>
	Median	60.5	61.0	
ECOG performance score, n (%)	0	30 (57.7%)	44 (73.3%)	0.218 <sup>x²</sup>
	1	18 (34.6%)	13 (21.7%)	
	2	4 (7.7%)	3 (5.0%)	
Menopausal status, n (%)	Premenopausal	13 (25.0%)	20 (33.3%)	0.335 <sup>x²</sup>
	Postmenopausal	39 (75.0%)	40 (66.7%)	
Histological type, n (%)	Ductal	26 (50.0%)	26 (43.3%)	0.394 <sup>x²</sup>
	Lobular	5 (9.6%)	3 (5.0%)	
	NST	21 (40.4%)	31 (51.7%)	
Ki-67 (%)	Median	25.0	20.0	0.943 <sup>m</sup>
	Mean $\pm$ SD	27.2 $\pm$ 16.2	28.0 $\pm$ 18.6	
ER status	Median (%)	90.0	90.0	0.817 <sup>m</sup>
	Mean $\pm$ SD	85.1 $\pm$ 18.1	86.6 $\pm$ 17.3	
PR status, n (%)	Positive	41 (78.8%)	54 (90.0%)	0.101 <sup>x²</sup>
	Negative	11 (21.2%)	6 (10.0%)	
PR percentage	Median (%)	30.0	60.0	0.061 <sup>m</sup>
	Mean $\pm$ SD	39.1 $\pm$ 35.4	51.1 $\pm$ 34.0	
Metastatic status, n (%)	<i>De novo</i> metastatic	26 (50.0%)	33 (55.0%)	0.597 <sup>x²</sup>
	Not <i>de novo</i>	26 (50.0%)	27 (45.0%)	
Metastatic sites, n (%)	Liver metastasis	14 (26.9%)	11 (18.3%)	0.276 <sup>x²</sup>
	Absent	38 (73.1%)	49 (81.7%)	
	Isolated bone metastasis	19 (36.5%)	16 (26.7%)	0.261 <sup>x²</sup>
Endocrine resistance, n (%)	Endocrine-sensitive	40 (76.9%)	49 (81.7%)	0.535 <sup>x²</sup>
	Endocrine-resistant	12 (23.1%)	11 (18.3%)	
Treatment, n (%)	Chemotherapy	11 (21.2%)	18 (30.0%)	0.286 <sup>x²</sup>
	Hormone therapy	41 (78.8%)	42 (70.0%)	
Progression-free survival (PFS)	Median PFS (months)	16.1	20.3	0.214
Overall survival (OS)	Median OS (months)	38.1	37.5	0.308
Progression status, n (%)	Present	39 (75.0%)	33 (55.0%)	0.028 <sup>x²</sup>
	Absent	13 (25.0%)	27 (45.0%)	
Survival status, n (%)	Deceased	23 (44.2%)	17 (28.3%)	0.080 <sup>x²</sup>
	Alive	29 (55.8%)	43 (71.7%)	
Follow-up duration (months)	Mean $\pm$ SD	27.0 $\pm$ 13.9	24.5 $\pm$ 10.6	0.278 <sup>t</sup>
	Median	26.3	23.0	

<sup>t</sup>: Independent samples t-test; <sup>x²</sup>: Chi-square test; <sup>m</sup>: Mann-Whitney U test; CI: Confidence interval; SD: Standard deviation; ER: Estrogen receptor; PR: Progesterone receptor; NST: No special type; ECOG: Eastern Cooperative Oncology Group.

in the palbociclib group and 18.3% in the ribociclib group. No statistically significant differences were noted in these characteristics between groups (Table 2).

In terms of survival outcomes, the median PFS was 16.1 months in the palbociclib group [95% confidence interval (CI): 19-29] and 20.3 months in the ribociclib group (95% CI: 22-30), with a p-value of 0.214. Median OS was 38.1 months in the palbociclib group (95% CI: 32-44) and 37.5 months in the ribociclib group (95% CI: 33-42), with a p-value of 0.308 (Figure 1).

ECOG performance status was identified as an independent prognostic factor for both PFS and OS in multivariate analysis (hazard ratio: 1.86, 95% CI: 1.18-2.94,  $p=0.028$ ). Subgroup analysis revealed that PFS and OS were longer in endocrine-

sensitive patients compared to endocrine-resistant ones, and in those receiving hormone therapy than chemotherapy. However, these differences did not reach statistical significance (Table 3 and Figure 2).

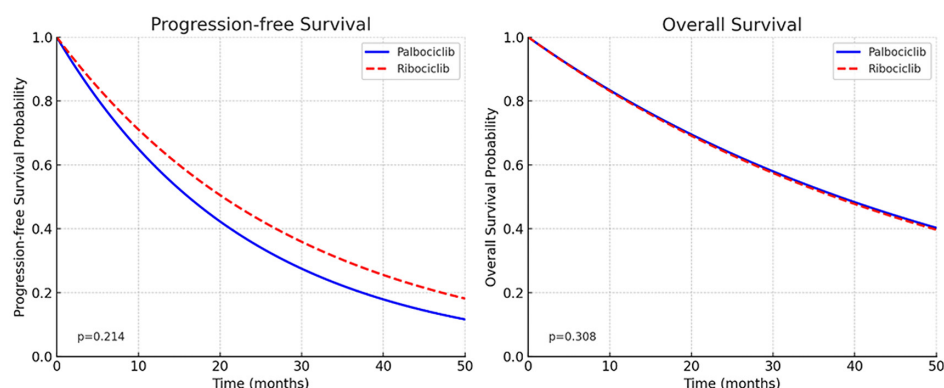
## DISCUSSION

This study aimed to compare the efficacy and safety of palbociclib and ribociclib in the second-line treatment of HR+, HER2-negative MBC. Our findings suggest that both drugs exhibit similar efficacy profiles in terms of PFS and OS, which is consistent with results from prior real-world studies. These results highlight the potential of both agents as viable options for second-line therapy in MBC patients, particularly those who are not suitable for chemotherapy.

**TABLE 2: Multivariate Cox analysis.**

Variable	Subgroup	HR	95% CI	p-value
Age	<65 years (reference)	1.0		
	≥65 years	1.24	0.92-1.67	0.156
ECOG performance score	0-1 (reference)	1.0		
	2	1.86	1.18-2.94	0.028
Menopausal status	Premenopausal (reference)	1.0		
	Postmenopausal	1.15	0.84-1.58	0.335
Histological type	Ductal (reference)	1.0		
	Lobular	1.22	0.73-2.04	0.394
	NST	1.18	0.88-1.58	0.394
ER percentage	≥90% (reference)	1.0		
	<90%	1.06	0.78-1.44	0.817
PR status	Positive (reference)	1.0		
	Negative	1.47	0.98-2.21	0.101
Ki-67 percentage	<20% (reference)	1.0		
	≥20%	1.02	0.75-1.39	0.943
<i>De novo</i> metastatic	No (reference)	1.0		
	Yes	1.12	0.83-1.51	0.597
Liver metastasis	Absent (reference)	1.0		
	Present	1.31	0.95-1.81	0.276
Isolated bone metastasis	Absent (reference)	1.0		
	Present	0.85	0.62-1.17	0.261
Number of metastatic sites	1-2 sites (reference)	1.0		
	≥3 sites	1.09	0.81-1.47	0.669
Endocrine resistance	Sensitive (reference)	1.0		
	Resistant	1.14	0.81-1.61	0.535
Previous treatment type	Hormone therapy (reference)	1.0		
	Chemotherapy	1.29	0.94-1.77	0.286

HR represents the risk ratio; CI;  $p<0.05$  is considered statistically significant; ECOG performance status was identified as a prognostic factor in the Cox regression model ( $p=0.028$ ); no statistically significant difference was found for other factors ( $p>0.05$ ); HR >1 indicates an association with poor prognosis, whereas HR <1 indicates a favorable prognosis; HR: Hazard ratio; CI: Confidence interval; ER: Estrogen receptor; PR: Progesterone receptor; NST: No special type; ECOG: Eastern Cooperative Oncology Group.

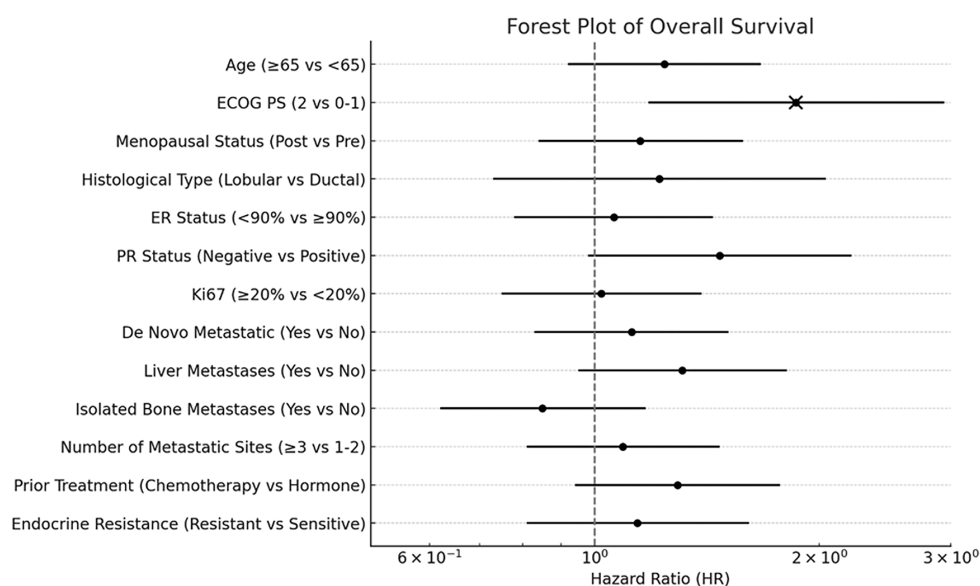


**FIGURE 1:** Kaplan-Meier survival curves comparing palbociclib and ribociclib in second-line treatment: Progression-free survival showed median durations of 16.1 vs 20.3 months ( $p=0.214$ ) and overall survival showed median durations of 38.1 vs 37.5 months ( $p=0.308$ ) for palbociclib and ribociclib arms, respectively.

**TABLE 3.** Subgroup analyses.

Subgroup	Category	Palbociclib (n=52)	Ribociclib (n=60)	p-value
Age groups	<65 years			0.616 <sup>†</sup>
	n (%)	28 (53.8%)	39 (65.0%)	
	Median PFS (months)	23.6	26.0	0.214
	Median OS (months)	38.1	37.5	0.308
	≥65 years			
	n (%)	24 (46.2%)	21 (35.0%)	
	Median PFS (months)	24.0	25.8	0.225
	Median OS (months)	37.2	36.9	0.412
Metastatic pattern	Visceral (liver/lung)			0.276 <sup>χ²</sup>
	n (%)	23 (44.2%)	26 (43.3%)	
	Median PFS (months)	22.4	25.2	0.198
	Median OS (months)	36.8	37.1	0.445
	Non-visceral (isolated bone)			0.261 <sup>χ²</sup>
	n (%)	19 (36.5%)	16 (26.7%)	
	Median PFS (months)	24.8	26.4	0.324
	Median OS (months)	39.2	38.6	0.512
Endocrine resistance status	Endocrine-sensitive			0.535 <sup>χ²</sup>
	n (%)	40 (76.9%)	49 (81.7%)	
	Median PFS (months)	25.2	27.3	0.187
	Median OS (months)	39.4	38.9	0.623
	Endocrine-resistant			
	n (%)	12 (23.1%)	11 (18.3%)	
	Median PFS (months)	20.8	23.1	0.144
	Median OS (months)	35.2	34.8	0.556
Previous treatment type	Chemotherapy			0.286 <sup>χ²</sup>
	n (%)	11 (21.2%)	18 (30.0%)	
	Median PFS (months)	21.4	24.2	0.167
	Median OS (months)	35.8	36.2	0.478
	Hormone therapy			
	n (%)	41 (78.8%)	42 (70.0%)	
	Median PFS (months)	24.6	26.8	0.198
	Median OS (months)	38.9	38.4	0.534

<sup>†</sup>: Independent samples t-test; <sup>χ²</sup>: Chi-square test; PFS: Progression-free survival; OS: Overall survival.



**FIGURE 2:** Forest plot of overall survival: Hazard ratios with 95% confidence intervals for various subgroups. The vertical dashed line represents HR =1, indicating no effect. Filled black squares denote statistically significant results ( $p < 0.05$ ).

HR: Hazard ratio; ER: Estrogen receptor; PR: Progesterone receptor; ECOG: Eastern Cooperative Oncology Group.

The characteristics of our patient population align with those reported in other real-world studies.<sup>8,10</sup> The mean age of patients in both treatment groups was similar, with a slight predominance of postmenopausal women in both cohorts. This finding is consistent with data suggesting that CDK4/6 inhibitors are commonly used in postmenopausal patients with HR+ breast cancer due to the more favourable hormonal milieu in this population. Moreover, the majority of patients in both treatment arms had ECOG performance scores of 0 or 1, indicating that the patients in our study were generally in good clinical condition, which is a typical characteristic of those enrolled in CDK4/6 inhibitor trials. In terms of survival outcomes, our study found no significant differences between the palbociclib and ribociclib arms in both median PFS (16.1 vs. 20.3 months,  $p=0.214$ ), and median OS (38.1 vs. 37.5 months,  $p=0.308$ ). This result mirrors findings from other studies, including the OPAL registry, which reported no significant survival advantage between palbociclib and ribociclib when used in second-line treatment for HR+, HER2-negative MBC.<sup>11,12</sup> Additionally, the indirect comparison by Petrelli et al.<sup>14</sup> and the paired study by Tremblay et al.<sup>15</sup> also supports the notion that palbociclib and ribociclib have comparable efficacy in clinical practice.<sup>13</sup> These findings are particularly relevant given the lack of randomized controlled trials directly comparing these two agents. Our results further emphasize that both drugs can be considered equivalent options in the second-line treatment of HR+, HER2-negative MBC, in line with current clinical practice guidelines.

The results of our multivariate analysis indicated that ECOG performance status was the only independent prognostic factor influencing both PFS and OS. This finding is consistent with real-world data, where performance status has been identified as a critical determinant of treatment outcomes in patients with MBC.<sup>15</sup> While other factors such as age, menopausal status, and metastasis type were associated with poorer outcomes in univariate analysis, they did not reach statistical significance in the multivariate model. This underscores the importance of patient performance status in clinical decision-making and highlights the need for tailored treatment strategies that consider individual patient characteristics.

The efficacy of CDK4/6 inhibitors may vary in patient subgroups, but generally provides benefit regardless of age and menopausal status.<sup>16</sup> A study in an Asian population showed that the presence of liver metastases was a particularly poor prognostic factor.<sup>17</sup> In our study, although the presence of liver metastasis appeared to be a negative factor in univariate analysis, it lost its statistical significance in multivariate analysis. The presence of visceral metastasis, especially liver metastasis, was associated with short PFS, but this finding did not reach statistical significance in our study.<sup>18</sup>

Interestingly, while ribociclib appeared to provide slightly better PFS in patients with visceral metastases, this difference did not achieve statistical significance in our study. This contrasts with findings from other studies, such as the trial by Ahmed Shaaban et al.<sup>12</sup>, which reported that ribociclib might



offer a greater benefit for patients with visceral disease.<sup>11</sup> This suggests that while ribociclib may have specific advantages in certain patient subgroups, the overall clinical benefit of palbociclib and ribociclib remains similar in most patients with HR+, HER2-negative MBC. While the results of our subgroup analyses are similar to other studies in the literature, they differ in some aspects. In a large-scale real-life study including 701 patients, no significant difference in treatment efficacy was found, similar to our findings, in subgroup analyses according to ER expression levels.<sup>19</sup> A study yielded data contradictory to ours, revealing a trend towards extended PFS in patients with *de novo* metastatic disease; however, the observed difference lacked statistical significance.<sup>20</sup> In a recent study, significant differences were reported in terms of ECOG performance status and *de novo* metastatic disease rates according to the stage of CDK4/6 inhibitor use.<sup>1</sup> Unlike our study, there is also a meta-analysis that reported that patients under 65 years of age and without visceral metastases benefited more from treatment.<sup>21</sup>

The fact that both drugs showed a similar efficacy profile in endocrine-sensitive and endocrine-resistant subgroups is an important finding. Previous studies have suggested that CDK4/6 inhibitors are particularly effective in endocrine-sensitive patients,<sup>22-24</sup> but our results support the growing body of evidence suggesting that even in endocrine-resistant settings, these agents continue to provide significant clinical benefits. In fact, the combination of CDK4/6 inhibitors with endocrine therapy remains a standard of care in MBC, and it is increasingly being used in patients with endocrine resistance, due to its favourable impact on quality of life and PFS compared to chemotherapy.<sup>23-25</sup> Our data further highlight the importance of using CDK4/6 inhibitors in a broad range of patients, including those with endocrine resistance.

One interesting observation from our study was the trend toward a more favorable PFS in the ribociclib arm during the later stages of the treatment course. Although this difference did not achieve statistical significance, it suggests that ribociclib may have a potential advantage in terms of long-term disease control, which warrants further investigation in larger, prospective trials. This finding is consistent with the previously reported differences in the pharmacokinetics and pharmacodynamics of palbociclib and ribociclib, particularly the longer half-life of ribociclib, which may contribute to a more sustained therapeutic effect.<sup>26</sup> However, the clinical relevance of this difference remains uncertain and requires further exploration in future studies.

## Study Limitations

One limitation of our study is its retrospective design and single-centre nature, which may introduce selection bias and limit the generalizability of the findings. Despite the inclusion of a substantial cohort of patients (n=112), multicenter, prospective trials, with larger sample sizes, might provide more reliable evidence. The lack of comprehensive data on post-progression therapies and BRCA mutation status represents a significant limitation of our study, as these factors may have influenced OS outcomes. Furthermore, while we assessed several clinical and pathological factors that may influence treatment response, the mechanisms underlying resistance to CDK4/6 inhibitors remain poorly understood, and further investigation is required. Biomarker-driven studies exploring resistance mechanisms, such as alterations in the retinoblastoma pathway, cyclin E, or other cell cycle regulators, may provide valuable insights into optimizing treatment strategies for this patient population.<sup>9</sup> Additionally, future studies should evaluate the quality of life and cost-effectiveness of palbociclib and ribociclib in second-line treatment, as these factors will play an important role in decision-making, especially in resource-constrained settings.

## CONCLUSION

Our study suggests that palbociclib and ribociclib are similarly effective in the second-line treatment of HR+, HER2-negative MBC. Although we found no statistically significant differences between the two agents in terms of survival outcomes, patient performance status emerged as a key determinant of treatment efficacy. Given the similar efficacy profiles, clinicians may consider individual patient characteristics, side effect profiles, and cost when choosing between these two drugs. Future studies, particularly those focused on biomarkers and resistance mechanisms, are needed to better understand how to optimize treatment for patients with MBC.

## Ethics

**Ethics Committee Approval:** The study was approved by the ethics committee of University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital Scientific Research Ethics Board (decision no: 2025/010.99/12/25, date: 24.01.2025) and conducted in accordance with the principles outlined in the Declaration of Helsinki.

**Informed Consent:** Retrospective study.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: S.Y., Ö.N.S., G.A.T., S.O., M.A., E.T., A.T., T.B., H.O., N.T., Concept: S.Y., Ö.N.S., G.A.T., S.O., M.A., E.T., A.T., T.B., H.O., N.T., Design: S.Y., Ö.N.S., G.A.T., S.O., M.A.,

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