Real World Outcomes of Patients Treated with the Oral CDK4/6 Inhibitors Ribociclib and Palbociclib: A Retrospective Study.

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Introduction

- Approximately 75% of patients with metastatic breast cancer have hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2-) disease (1).
- Randomized phase III trials have established the CDK4/6 inhibitors (CDK4/6i) palbociclib (PALOMA-2) and ribociclib (MONALEESA-2) in combination with endocrine therapy as the standard of care in HR+/HER2- metastatic breast cancer (2)(3).
- Despite robust results, clinical trial populations may not fully reflect real-world practice, where patient comorbidities, treatment adherence, and adverse events management can influence outcomes.
- This study aimed to describe real-world treatment patterns, tolerability, and progression free survival (PFS) outcomes amongst patients treated with palbociclib or ribociclib.

Aim

- To assess real-world rates of dose reductions, dose delays and discontinuation during treatment with ribociclib or palbociclib for metastatic breast cancer.
- To evaluate progression-free survival for both agents.

Methods

- Single centre retrospective chart review conducted between June 1st, 2014, and June 1st, 2024, at the Bons Secours Cork Cancer Centre, Ireland.
- Included patients treated with either palbociclib or ribociclib in combination with endocrine therapy for HR+/HER2- metastatic or unresectable advanced breast cancer.
- Variables collected included demographics, disease characteristics, and treatment-related information such as CDK4/6i type, initiation dose and concurrent endocrine therapy.
- Treatment tolerability was assessed through dose modifications, dose delays and treatment cessation, cycle and reason for change.
- Descriptive statistics were used to summarise patient demographics. Comparative analyses assessed differences dose modification, dose delays and treatment discontinuation.
- PFS was evaluated using Kaplan–Meier methodology, and subgroup analyses explored associations between baseline characteristics, treatment tolerability, and clinical outcomes.

Results

Demographics:

- 84 patients were included in this study ribociclib (n=40) and palbociclib (n=44) **Table 1.**
- Patients prescribed palbociclib were older at treatment initiation: mean age 68.0 years vs ribociclib 60.8 years *(p=0.007 t-test)* and had a higher rate of visceral metastasis 66% (n=29/44) vs 43% (n=17/40) *(p=0.03 chi²)*.

Treatment outcomes:

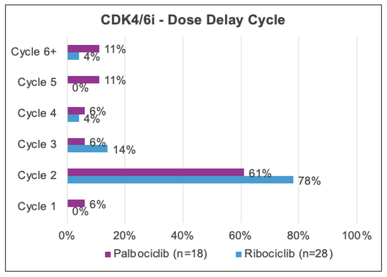
- 70% (n=28/40) of patients receiving ribociclib had a dose delay vs 41% (n=18/44) receiving palbociclib *(p=0.008 chi²)*. 65% (n=26/40) of patients on ribociclib had a dose reduction vs 32% (n=14/44) on palbociclib *(p=0.002 chi²)* **Table 2.**
- Reasons for dose reductions and delays are summarised in **Figure 1.**
- Approximately one third of patients discontinued their CDK4/6i in the first six cycles: 28% (n=11/40) on ribociclib and 36% (n=16/44) on palbociclib **Table 2.**

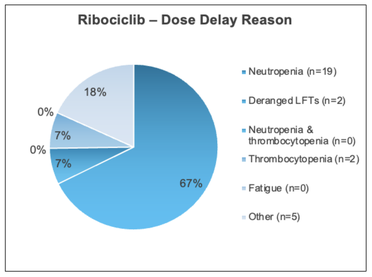
Progression free survival:

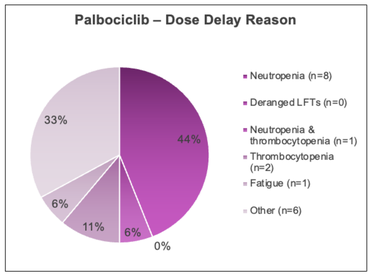
- 76 patients started CDK4/6i in the first line setting of which 38% (n=14/37) progressed on ribociclib and 61.5% (n=24/39) progressed on palbociclib.
- Median PFS for ribociclib was 47.0 months [95% CI 20.0 -47.9] versus 21.4 months [95% CI 5.02 – 88.8] on palbociclib.
- No statistically significant difference was observed between the two groups *(p=0.2)* **Figure 2.**

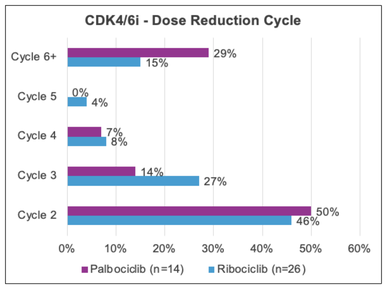
Table 1: Demographics

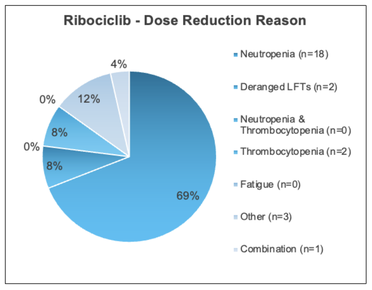
Characteristic	Ribociclib n (%)	Palbociclib n (%)	p-value
	n=40 (48%)	n=44 (52%)	
Age (Years) (Mean ± SD) [Range]			
Diagnosis of metastasis	60.8 ±11.9 [32-78]	68.0 ± 11.9 [43-86]	0.007 (t-test)
Initiation CDK4/6i	61.4 ±11.8	68.1 ±11.8	0.01 (t-test)
Menopausal status			
Pre menopause	7 (18%)	6 (14%)	0.57 (chi^2)
Post menopause	33 (82%)	37 (86%)	
Metastasis			
De novo	12 (30%)	16 (36%)	0.53 (chi^2)
Recurrence	28 (70%)	28 (64%)	
Visceral Metastasis	17 (43%)	29 (66%)	0.03 (chi^2)
Prior chemotherapy	20 (50%)	19 (43%)	0.5 (chi^2)
Comorbidities	8 (20%)	13 (30%)	0.39 (fishers)
Diabetes mellitus (DM)	1 (2.5%)	0 (0%)	
Cardiovascular Disease (CVD)	0 (0%)	3 (7%)	
Hypertension (HTN)	4 (10%)	8 (18.4%)	
DM & CVD	1 (2.5%)	1 (2.3%)	
CVD & HTN	1 (2.5%)	1 (2.3%)	
DM, CVD, HTN	1 (2.5%)	0 (0%)	
CDK4/6 Initial dose (Ribociclib/Palbociclib)			
Starting dose (600mg/125mg)	35 (88%)	43 (97%)	
Dose level -1 (400mg/100mg)	5 (12%)	0 (0%)	
Dose level -2 (200mg/75mg)	0 (0%)	1 (2%)	
Concurrent Therapy			
Letrozole	30 (75%)	25 (57%)	0.4 (fishers)
Fulvestrant	8 (20%)	14 (32%)	
Exemestane	1 (2.5%)	2 (4%)	
Anastrozole	1 (2.5%)	3 (7%)	











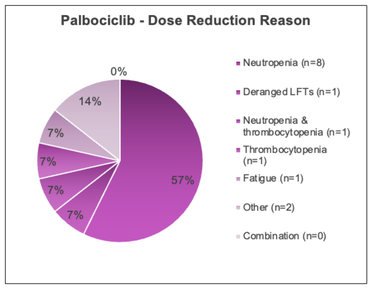


Figure 1: Dose delays and dose reductions – cycle and reason

Table 2: Treatment Outcomes

Characteristic	Ribociclib n (%)	Palbociclib n (%)	p-value
Dose delays	28/40 (70%)	18/44 (41%)	0.008 (chi^2)
Dose reductions	26/40 (65%)	14/44 (32%)	0.002 (chi^2)
Disease progression	14/40 (35%)	27/44 (61%)	
Discontinuation first six cycles	11/40 (28%)	16/44 (36%)	

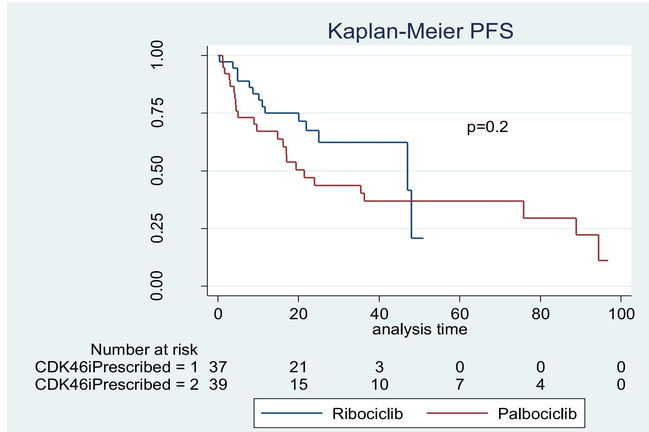


Figure 2: Kaplan Meier curve for patients receiving first line CDK4/6i for metastatic breast cancer

Conclusion

- Ribociclib was associated with higher rates of dose delays and dose reductions in our cohort.
- Reasons for dose delays and reductions for both CDK4/6i were in keeping with published adverse events i.e. neutropenia.
- Treatment discontinuation in the first six cycles was higher with palbociclib and a larger number progressed on this agent.
- Numerical trends towards improved event free survival favoured ribociclib, although this was not statistically significant, and a larger dataset may provide more information.

References

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