REAL WORLD OUTCOME DATA FROM THE GERMAN REGISTRY PLATFORM OPAL

PALBOCICLIB VERSUS RIBOCICLIB IN FIRST-LINE TREATMENT OF PATIENTS WITH HORMONE RECEPTOR-POSITIVE, HER2-NEGATIVE ADVANCED BREAST CANCER

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INTRODUCTION

CDK4/6 inhibitors (CDKi) plus endocrine therapy (ET) are standard of care in first-line treatment of hormone receptor-positive (HR+), HER2-negative (HER2-) advanced breast cancer (ABC). In the pivotal trials, the three CDKi (palbociclib, ribociclib and abemaciclib) + ET showed similar progression-free survival (PFS) benefit over ET alone. However, other than ribociclib, palbociclib failed to demonstrate a benefit in overall survival (OS). As patient characteristics differed between the trials, especially in the number of patients with treatment-free interval (TFI) of < 12 months after the end of adjuvant ET, head-to-head comparisons of the CDKi are of clinical interest. Here, we analyze the outcome of patients treated with palbociclib + ET or ribociclib + ET with real-world data from the OPAL breast cancer registry.

CONCLUSION

This analysis of real word data in the OPAL registry platform showed similar PFS and OS for palbociclib + ET compared to ribociclib + ET, when adjusted for a wide range of potential confounding variables. Further analyses will investigate whether one drug showed favorable results in certain subgroups of patients.

METHODS

OPAL (NCT03417115) is a prospective, observational, open, longitudinal multicenter cohort study (clinical registry) in Germany. Patients with ABC and early breast cancer can be recruited at the start of their first systemic treatment. There are no treatment restrictions. Sites from all medical sectors can participate in OPAL (medical and gynecologic oncologists from outpatient centers and clinics). Details on all (sequential) treatments, patient and tumor characteristics, biomarker testing, clinical and patient-reported outcomes are collected. Follow-up is up to 5 years.

Between 01/2018 and 07/2021 1049 patients with HR+ HER2- ABC were recruited by 143 sites. Database cut was on 31/08/2023. 388 patients received palbociclib + ET and 235 patients received ribociclib + ET as first-line treatment. All endocrine combination partners including switch of ET during first line therapy were allowed, whereas patients with documented switch of CDKi (n=28) were excluded.

PFS in registries can differ from PFS in clinical trials, since the RECIST criteria are usually not applied in routine care. PFS in registries represents the time to clinically relevant progression in routine care. PFS and OS were estimated using the Kaplan-Meier method.

To adjust for confounding, inverse probability of treatment weighting (IPTW) by propensity score analysis was used to compare PFS and OS between first-line palbociclib + ET and ribociclib + ET. IPTW was performed for the following variables: age, menopausal status, ECOG, any comorbidity, Charlson comorbidity index, metastatic stage, type of metastasis, number of metastatic sites, estrogen-/progesterone status, HER2 IHC status, previous chemo-/endocrine therapy, kind of endocrine combination partner, disease-free interval, and treatment-free interval (defined as time from end of (neo)adjuvant treatment until disease progression).

RESULTS

From 2018 to 2021, the proportion of CDKi increased from 68% to 86% in first-line treatment of HR+HER2- ABC. Overall, palbociclib was used in 44% and ribociclib in 26% of all first-line treatments in OPAL.

The median age of patients receiving palbociclib/ribociclib was 66 vs 68 years and most of the patients were postmenopausal at start of first-line treatment (79% vs 86%). For 77% vs 81% of patients at least one comorbidity was documented. 38% vs 35% of patients already had metastases at diagnosis (M1), and 25% vs 26% of patients had a TFI < 12 months. Pretreatment in the adjuvant setting with chemotherapy was documented for 38% vs 39% of the patients, and 53% vs 59% have received adjuvant endocrine therapy. At the start of first line treatment, 15% of patients in the palbociclib group had bone metastases only, compared to 20% of patients treated with ribociclib. 66% vs 71% received an aromatase inhibitor only, and 23% vs 21% fulvestrant only, as combination partner in first-line treatment. These and further patient, tumor and treatment characteristics are displayed in **Table 1 and Table 2**. After IPTW, the standardized mean difference was smaller than 0.1 for all tested characteristics except the category unknown prior endocrine therapy (n = 13, **Figure 1**). Therefore, we conclude that the two treatment groups are comparable.

51% vs 53% of patients had a progression (palbociclib/ribociclib group). The IPTW-adjusted median PFS was 26.7 months (95% Confidence interval (CI) 23.2 – 30.7) for the palbociclib and 27.0 months (95%-CI 21.1 – 30.7) for the ribociclib group **(Figure 2)**. The hazard ratio was 1.01 (0.80 – 1.26) for palbociclib versus ribociclib.

32% vs 34% of patients had an OS event (palbociclib/ribociclib group). IPTW-adjusted median OS was 41.4 months (95%-CI 38.8 – 50.3) for the palbociclib and 49.3 months (95%-CI 36.9 – NA) for the ribociclib group **(Figure 3)**. The hazard ratio was 0.99 (0.72 - 1.29) for palbociclib versus ribociclib.

Table 1: Patient and tumor characteristics

Characteristic	Palbociclib + ET	Ribociclib + ET	Total
Patients (N)	**388**	**235**	**623**
Age[1]			
Median	66.21	68.00	66.93
25%/75% quantiles	56.16 – 75.47	59.45 – 76.12	56.93 – 75.79
Menopausal status[1]			
Pre-menopausal	48 (12.4%)	19 (8.1%)	67 (10.8%)
Peri-menopausal	13 (3.4%)	7 (3.0%)	20 (3.2%)
Post-menopausal	306 (78.9%)	202 (86.0%)	508 (81.5%)
Unknown	21 (5.4%)	7 (3.0%)	28 (4.5%)
ECOG[1,2]			
0	163 (42.0%)	85 (36.2%)	248 (39.8%)
1	117 (30.2%)	92 (39.1%)	209 (33.5%)
≥2	39 (10.1%)	28 (11.9%)	67 (10.8%)
Unknown	69 (17.8%)	30 (12.8%)	99 (15.9%)
Any comorbidity[1,3]			
Yes	298 (76.8%)	191 (81.3%)	489 (78.5%)
No	90 (23.2%)	44 (18.7%)	134 (21.5%)
Charlson Comorbidity Index[1,4]			
0	311 (80.2%)	176 (74.9%)	487 (78.2%)
≥1	77 (19.8%)	59 (25.1%)	136 (21.8%)
Metastasis at diagnosis			
No (metachronous, M0)	240 (61.9%)	152 (64.7%)	392 (62.9%)
Yes (synchronous, M1)	146 (37.6%)	81 (34.5%)	227 (36.4%)
MX/Unknown	2 (0.5%)	2 (0.9%)	4 (0.6%)
Type of metastases[5]			
Bone only	57 (14.7%)	46 (19.6%)	103 (16.5%)
Non-visceral 6 and none-bone only	83 (21.4%)	42 (17.9%)	125 (20.1%)
Visceral ± non-visceral	200 (51.5%)	128 (54.5%)	328 (52.6%)
No documentation available	48 (12.4%)	19 (8.1%)	67 (10.8%)
Number of metastatic sites[1]			
1	143 (36.9%)	89 (37.9%)	232 (37.2%)
2	109 (28.1%)	75 (31.9%)	184 (29.5%)
≥ 3	88 (22.7%)	52 (22.1%)	140 (22.5%)
Unknown	48 (12.4%)	19 (8.1%)	67 (10.8%)
Hormone receptor[1]			
ER+/PR+	315 (81.2%)	174 (74.0%)	489 (78.5%)
ER+/PR-	70 (18.0%)	59 (25.1%)	129 (20.7%)
ER-/PR+	0 (0.0%)	1 (0.4%)	1 (0.2%)
HR+ not further specified (yet)	3 (0.8%)	1 (0.4%)	4 (0.6%)
HER2 IHC test result[1]			
0	135 (34.8%)	87 (37.0%)	222 (35.6%)
+/++	193 (49.7%)	111 47.2%)	304 (48.8%)
Unknown/Missing	60 (15.5%)	37 (15.7%)	97 (15.6%)

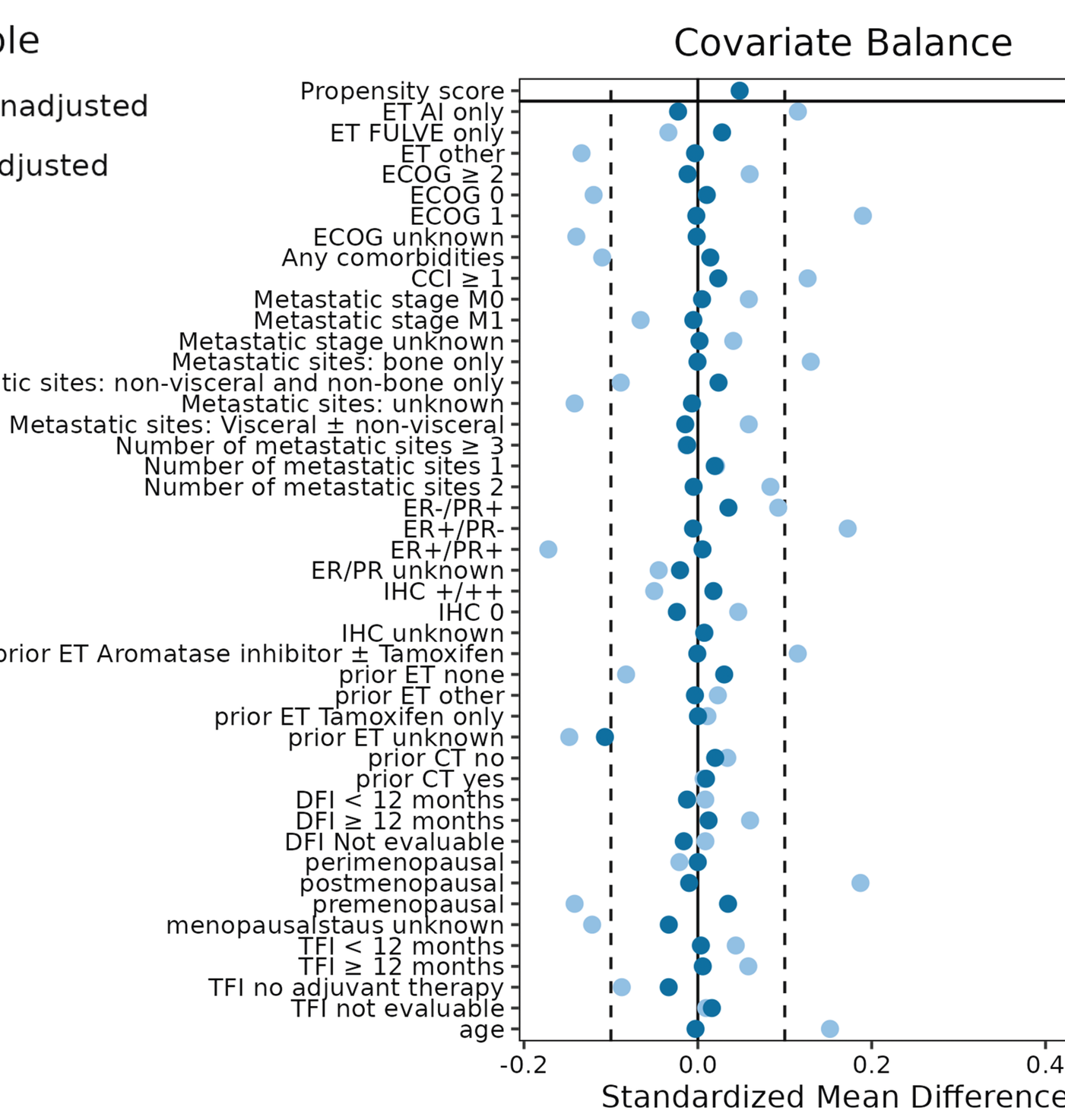
ER: estrogen receptor status
ET: endocrine therapy
HR: hormone receptor status
IHC: immunohistochemistry
PR: progesterone receptor status
[1] at start of first-line treatment
[2] ECOG: Eastern Cooperative Oncology Group (Oken et al. 1982).
[3] Any comorbidity: comorbidities according to CCI and other comorbidities combined.
[4] CCI: Comorbidities according to Charlson et al. 1987, current weighting according to Quan et al. 2011. Range 0-24.
[5] Metastasis at the start of therapy: Documented metastatic sites in the period from 8 weeks before to 4 weeks after the start of therapy.
[6] Non-visceral disease includes bone, soft tissue, skin and lymph node metastases. All other metastases are visceral.

Table 2: Treatment characteristics

Characteristic	Palbociclib + ET	Ribociclib + ET	Total
Patients (N)	**388**	**235**	**623**
Endocrine combination partner first-line			
Aromatase inhibitor only	255 (65.7%)	167 (71.1%)	422 (67.7%)
Fulvestrant only	88 (22.7%)	50 (21.3%)	138 (22.2%)
Other	45 (11.6%)	18 (7.7%)	63 (10.1%)
Previous chemotherapy			
Yes	149 (38.4%)	91 (38.7%)	240 (38.5%)
None	228 (58.8%)	142 (60.4%)	370 (59.4%)
Unknown/missing	11 (2.8%)	2 (0.9%)	13 (2.1%)
Previous endocrine therapy			
Aromatase inhibitor ± tamoxifen	113 (29.1%)	81 (34.5%)	194 (31.1%)
Tamoxifen only	89 (22.9%)	55 (23.4%)	144 (23.1%)
Others	4 (1.0%)	3 (1.3%)	7 (1.1%)
None	171 (44.1%)	94 (40.0%)	265 (42.5%)
Unknown/missing	11 (2.8%)	2 (0.9%)	13 (2.1%)
Disease -free interval			
≥ 12 months	228 (58.8%)	145 (61.7%)	373 (59.9%)
< 12 months	11 (2.8%)	7 (3.0%)	18 (2.9%)
Not evaluable	3 (0.8%)	2 (0.9%)	5 (0.8%)
De novo metastasis (M1 at diagnosis)	146 (37.6%)	81 (34.5%)	227 (36.4%)
Treatment-free interval			
≥ 12 months	99 (25.5%)	66 (28.1%)	165 (26.5%)
< 12 months	95 (24.5%)	62 (26.4%)	157 (25.2%)
Not evaluable	32 (8.2%)	20 (8.5%)	52 (8.3%)
De novo metastasis (M1 at diagnosis)	146 (37.6%)	81 (34.5%)	227 (36.4%)
No (neo)adjuvant therapy	16 (4.1%)	6 (2.6%)	22 (3.5%)

ET: endocrine therapy

Figure 1: Standardized mean differences between the two treatment groups before (unadjusted) and after IPTW (adjusted)



AI: aromatase inhibitor
CCI: Charlson Comorbidity Index
CT: chemotherapy
DFI: disease-free interval
ER: estrogen receptor status
ET: endocrine therapy
FUL: fulvestrant
IHC: immunohistochemistry
PR: progesterone receptor status
TFI: treatment-free interval

Figure 2: Progression-free survival of patients with palbociclib+ET/ribociclib+ET in first-line after IPTW

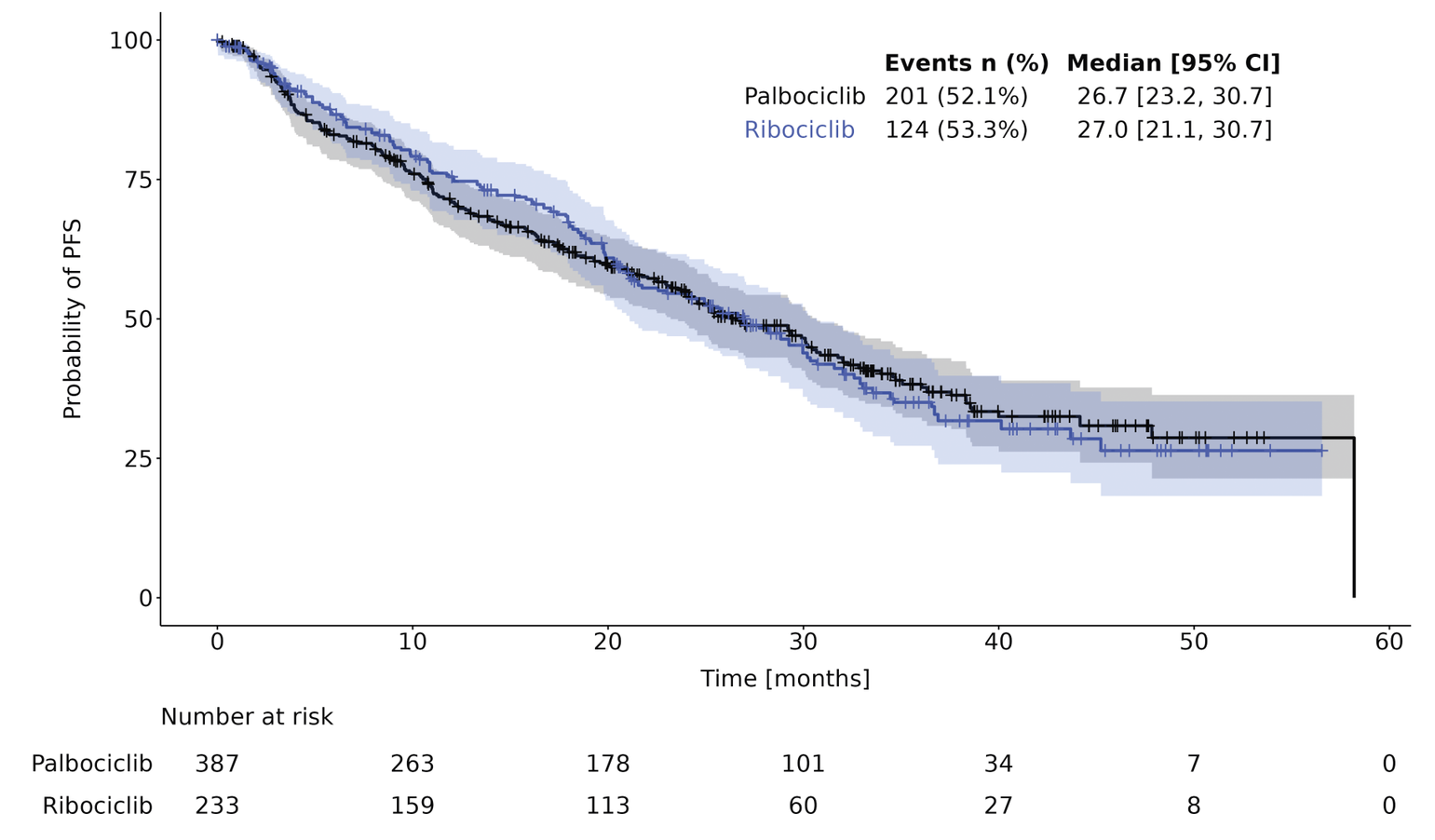
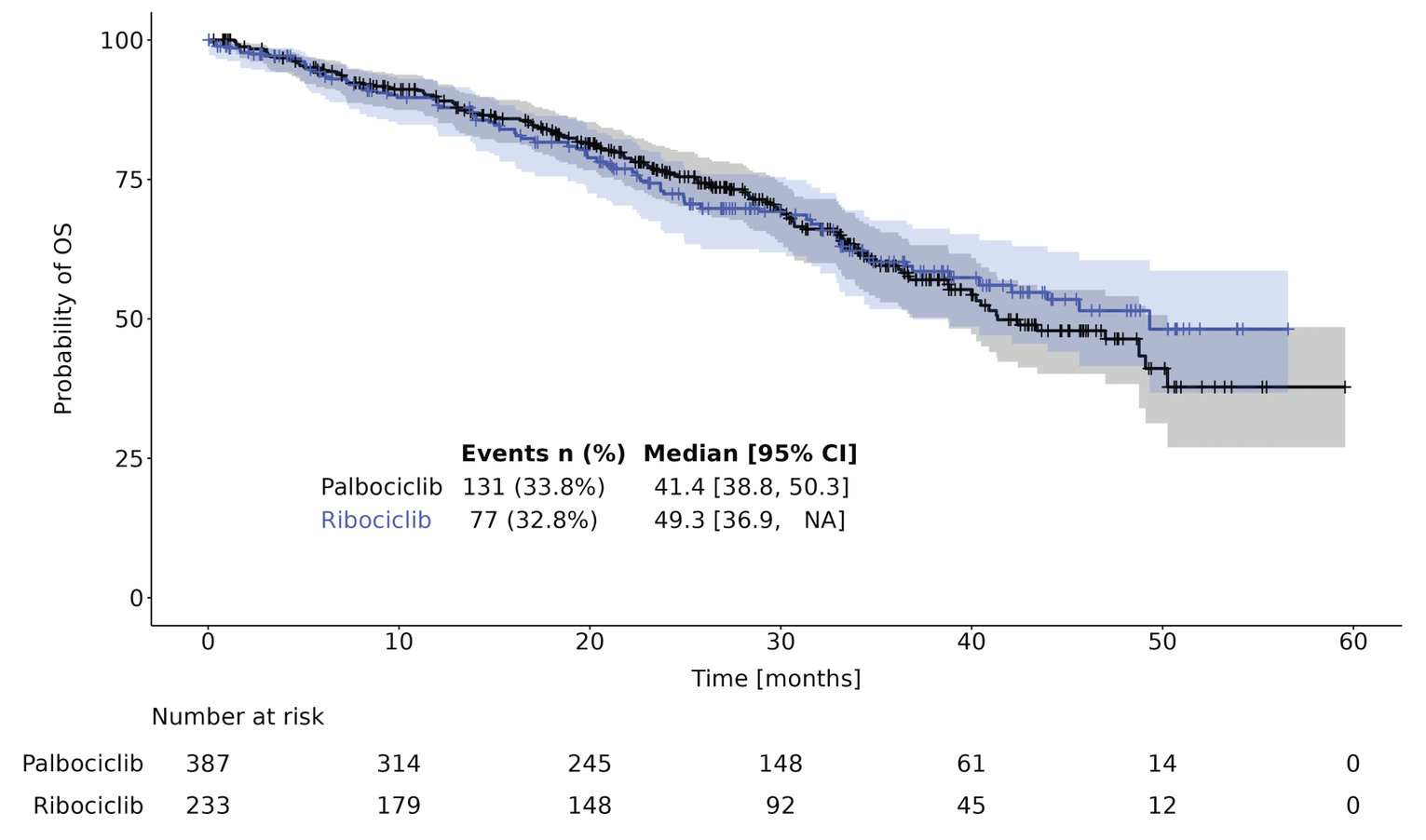


Figure 3: Overall survival of patients with palbociclib+ET/ribociclib+ET in first-line after IPTW



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