Supplementary Online Content

This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Incidence of Progression-Free Survival and Overall Survival

	Concomitant PPI (n=344)			Non-concomitant PPI (n=966)			Absolute risk difference	Relative risk ratio
	Events	Person-years	Incidence rate	Events	Person-years	Incidence rate		
Real-world progression-free survival	160	459	0.35 (0.29-0.40)	319	1,595	0.20 (0.18-0.22)	0.15 (0.09-0.21)	1.74 (1.44-2.11)
Overall survival	102	604	0.17 (0.14-0.20)	118	1,881	0.06 (0.05-0.07)	0.11 (0.07-0.14)	2.69 (2.07-3.51)

PPI: proton pump inhibitor

eTable 2. Adjusted Hazard Ratio of Progression-Free Survival and Overall Survival

	Hazard ratio (95% CI)	
Covariates	Real-world progression-free survival	Overall survival
Concomitant proton pump inhibitor		
No	1.00	1.00
Yes	**1.76 (1.46–2.13)**	**2.71 (2.07–3.53)**
Treatment combination		
palbociclib+anastrozole/letrozole	1.00	1.00
palbociclib+fulvestrant	**2.23 (1.68–2.95)**	**2.18 (1.44–3.30)**
Age		
<50	1.00	1.00
≥50	0.91 (0.71–1.17)	1.38 (0.90–2.11)
Charlson comorbidity index	1.02 (0.99–1.04)	1.01 (0.97–1.06)
Menopause		
No	1.00	1.00
Yes	1.20 (0.55–2.65)	1.51 (0.36–6.39)
Prior chemotherapy		
No	1.00	1.00
Yes	0.83 (0.33–2.05)	0.68 (0.16–2.81)
Prior endocrine therapy		
No	1.00	1.00
Yes	0.80 (0.53–1.22)	0.71 (0.36–1.41)

Bold indicates *P*-value < 0.05.

eTable 3. Baseline Demographics and Clinical Characteristics After 1:5 Propensity Score Matching

	Concomitant PPI group (N = 344)	Non-concomitant PPI group (N = 1,587)	P-value[1]	SMD
Age, n (%)			0.0686	0.11
<50	53 (15.41)	313 (19.72)		
≥50	291 (84.59)	1274 (80.28)		
Menopause, n (%)			0.6183	-0.03
Yes	338 (98.26)	1565 (98.61)		
No	6 (1.74)	22 (1.39)		
Treatment combination, n (%)			0.4717	-0.05
anastrozole/letrozole	292 (84.88)	1319 (83.11)		
fulvestrant	52 (15.12)	268 (16.89)		
CCI, mean (SD)	5.40 (3.38)	4.80 (3.42)	0.0033	0.17
Prior chemotherapy, n (%)			1.00	-0.03
Yes	4 (1.16)	23 (1.45)		
No	340 (98.84)	1564 (98.55)		
Prior endocrine therapy, n (%)			1.00	-0.01
Yes	20 (5.81)	95 (5.99)		
No	24 (94.19)	492 (94.01)		
Any metastasis, (%)	174 (50.58)	813 (51.23)	0.5524	0.04
Bone[2]	104 (30.23)	411 (25.90)	0.1065	0.10
Lung[2]	44 (12.79)	242 (15.25)	0.2764	-0.07
Brain[2]	9 (2.62)	25 (1.58)	0.1785	0.07
Liver[2]	15 (4.36)	78 (4.91)	0.7813	-0.03
Other sites[2]	23 (6.69)	90 (5.67)	0.4488	0.04

[1] The *P*-value of the difference between the concomitant and non-concomitant groups was determined using Student's t-tests and Chi-squared tests.
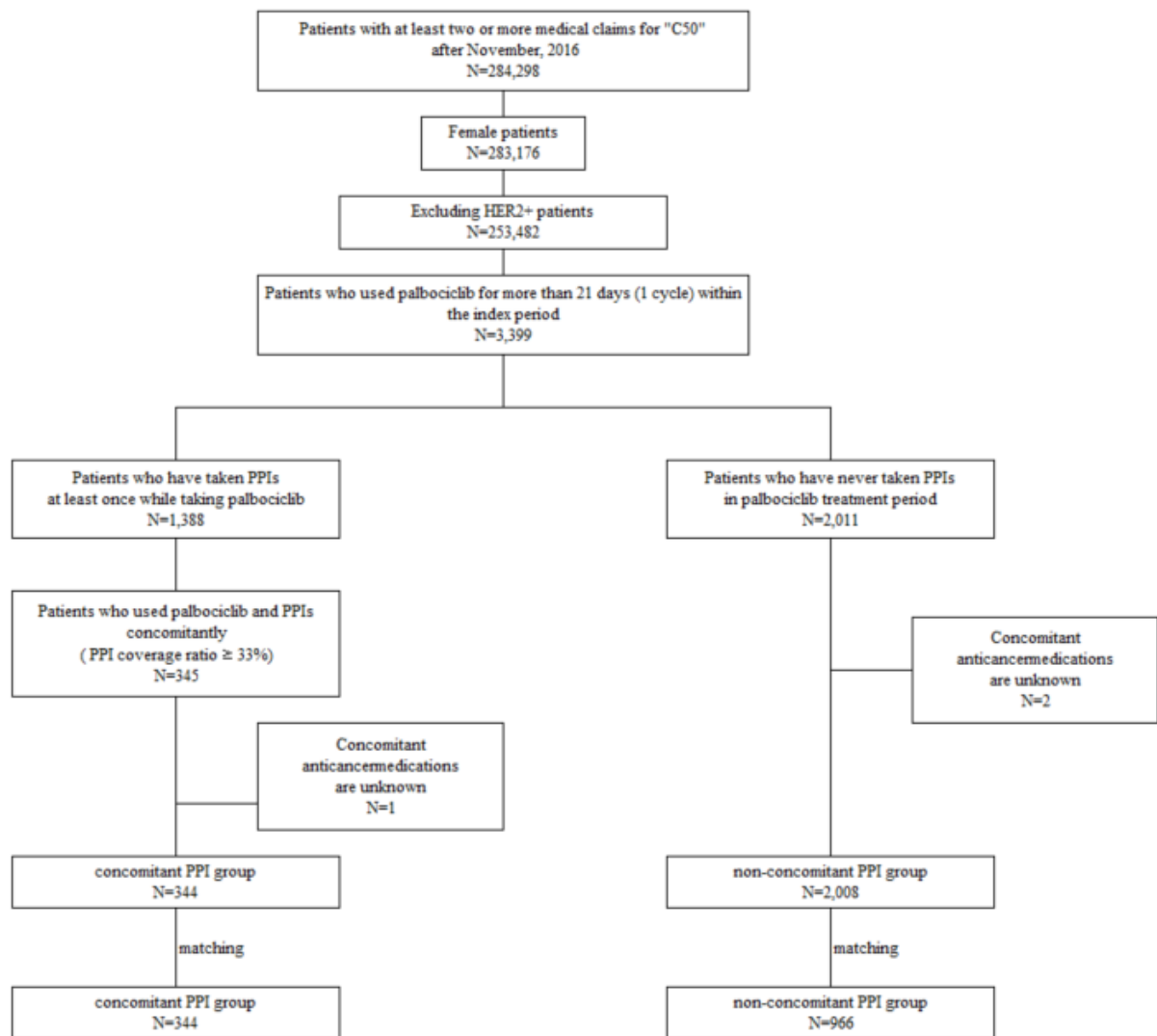[2] Variables were not used to match two groups
PPI: proton pump inhibitor, SD: standard deviation, SMD: standardized mean difference
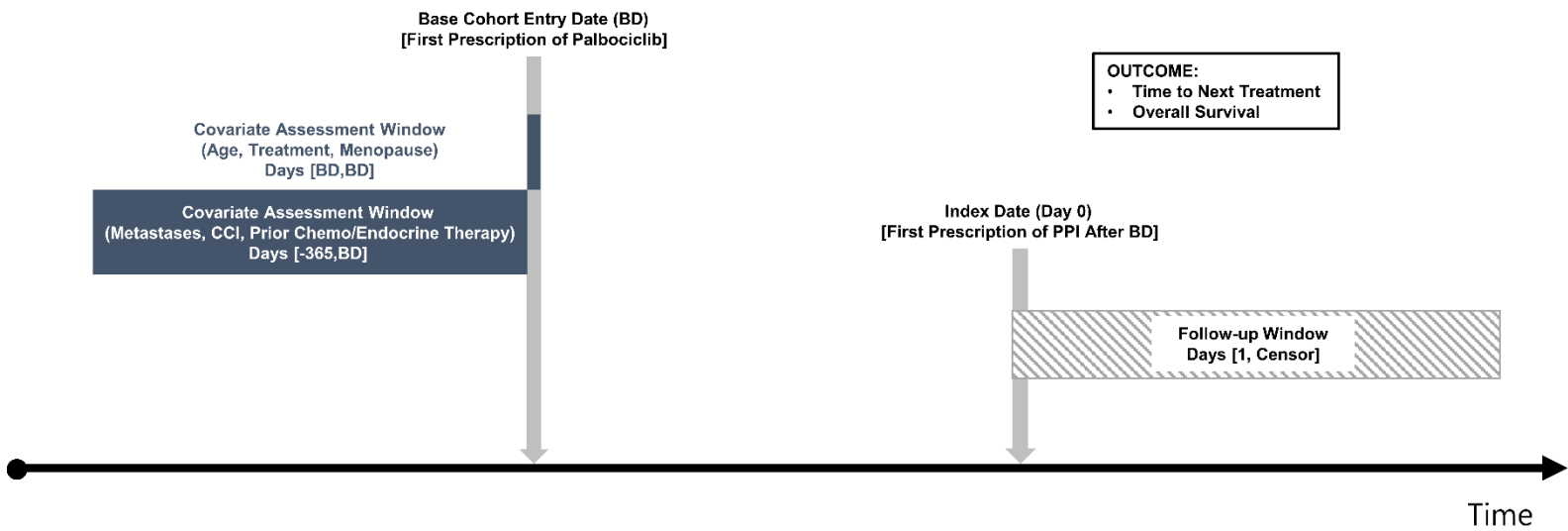
eTable 4. Adjusted Hazard Ratio of Progression-Free Survival and Overall Survival From 1:5 Matched Cohort

Covariates	Hazard ratio (95% CI)	
	Real-world progression-free survival	Overall survival
Concomitant proton pump inhibitor		
No	1.00	1.00
Yes	1.87 (1.59–2.20)	2.76 (2.16–3.52)
Treatment combination		
palbociclib+anastrozole/letrozole	1.00	1.00
palbociclib+fulvestrant	1.94 (1.57–2.40)	2.13 (1.49–3.02)
Age		
<50	1.00	1.00
≥50	1.02 (0.85–1.24)	1.36 (0.96–1.92)
Charlson comorbidity index	1.01 (0.99–1.03)	1.01 (0.97–1.04)
Menopause		
No	1.00	1.00
Yes	1.36 (0.69–2.69)	1.89 (0.45–7.86)
Prior chemotherapy		
No	1.00	1.00
Yes	1.02 (0.58–1.79)	1.27 (0.55–2.93)
Prior endocrine therapy		
No	1.00	1.00
Yes	0.97 (0.71–1.31)	0.82 (0.47–1.41)

eFigure 1. Patient Selection Flowchart

eFigure 2. Study Design

Base Cohort Entry Date (BD)
[First Prescription of Palbociclib]

OUTCOME:
• Time to Next Treatment
• Overall Survival

Covariate Assessment Window
(Age, Treatment, Menopause)
Days [BD,BD]

Covariate Assessment Window
(Metastases, CCI, Prior Chemo/Endocrine Therapy)
Days [-365,BD]

Index Date (Day 0)
[First Prescription of PPI After BD]

Follow-up Window
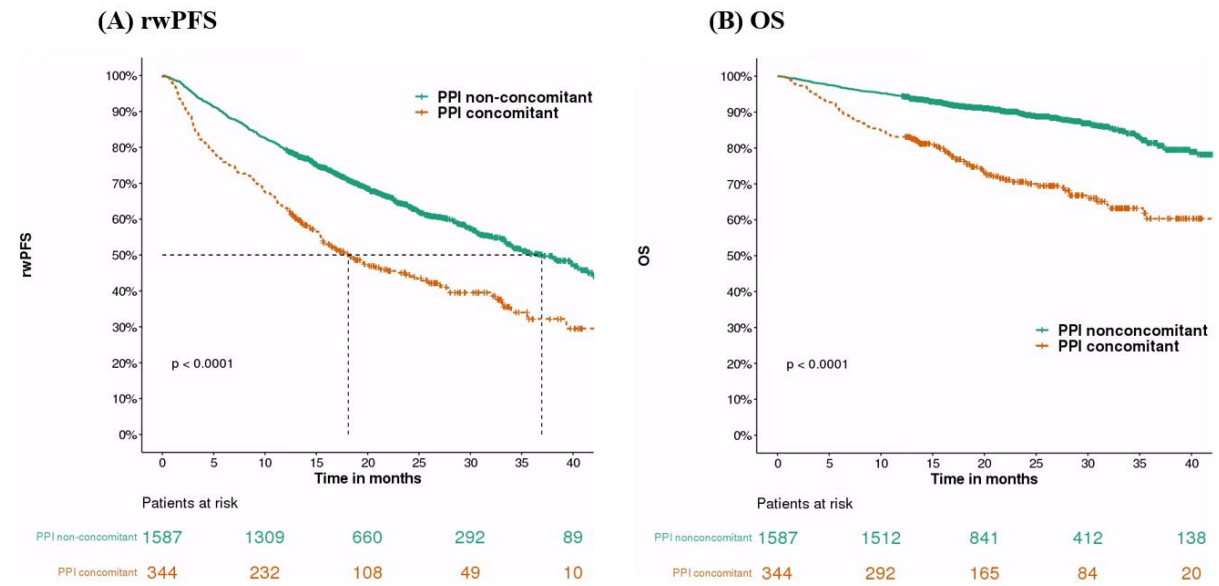Days [1, Censor]

Time

eFigure 3. Assigning Index Date of Patients With Nonconcomitant PPI
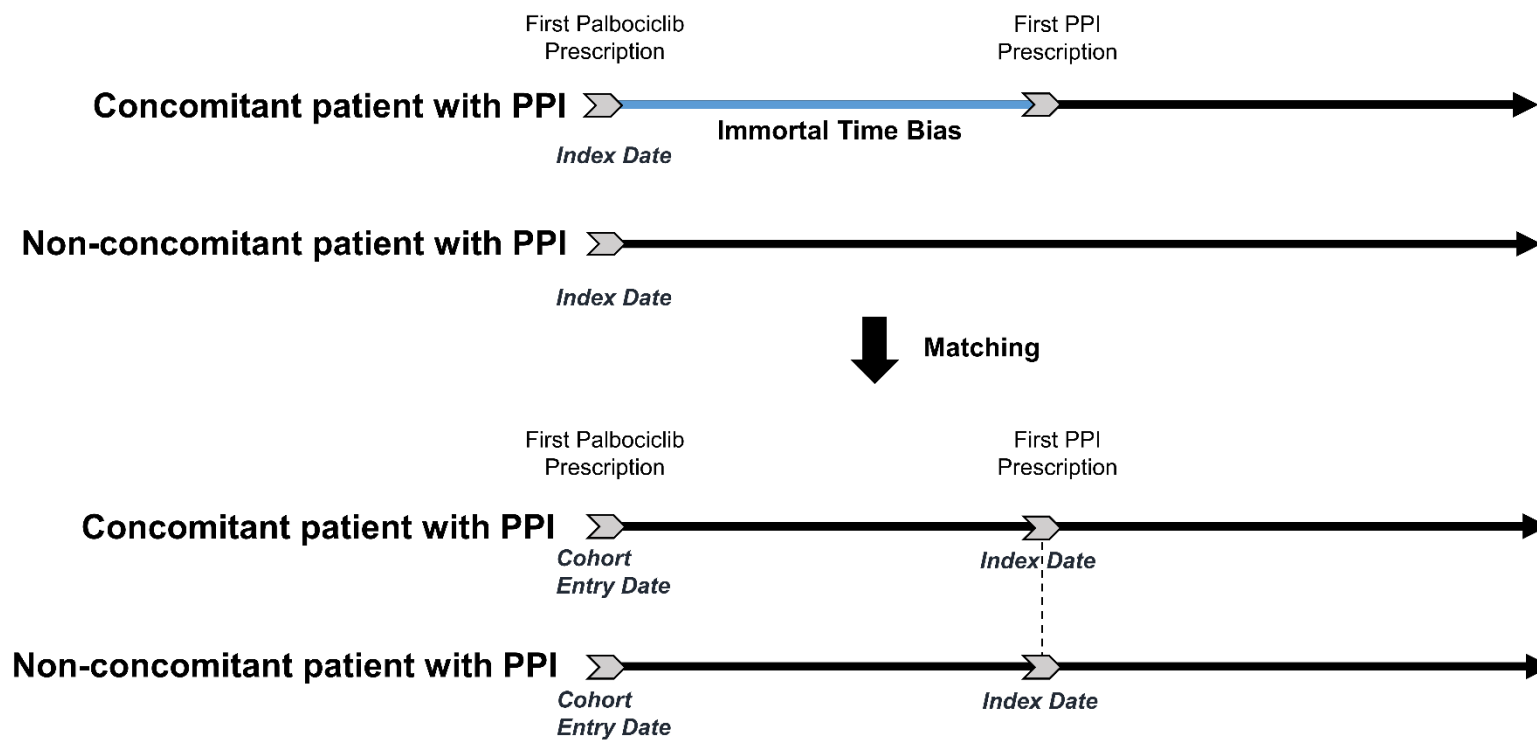
eFigure 4. Progression-Free Survival and Overall Survival of Concomitant PPI Group and Nonconcomitant PPI Group From 1:5 Matched Cohort

(A) rwPFS

(B) OS

eFigure 5. Progression-Free Survival in Patients With Endocrine-Sensitive and Endocrine-Resistant Treatment From 1:5 Matched Cohort

(A) Endocrine sensitive

(B) Endocrine resistant
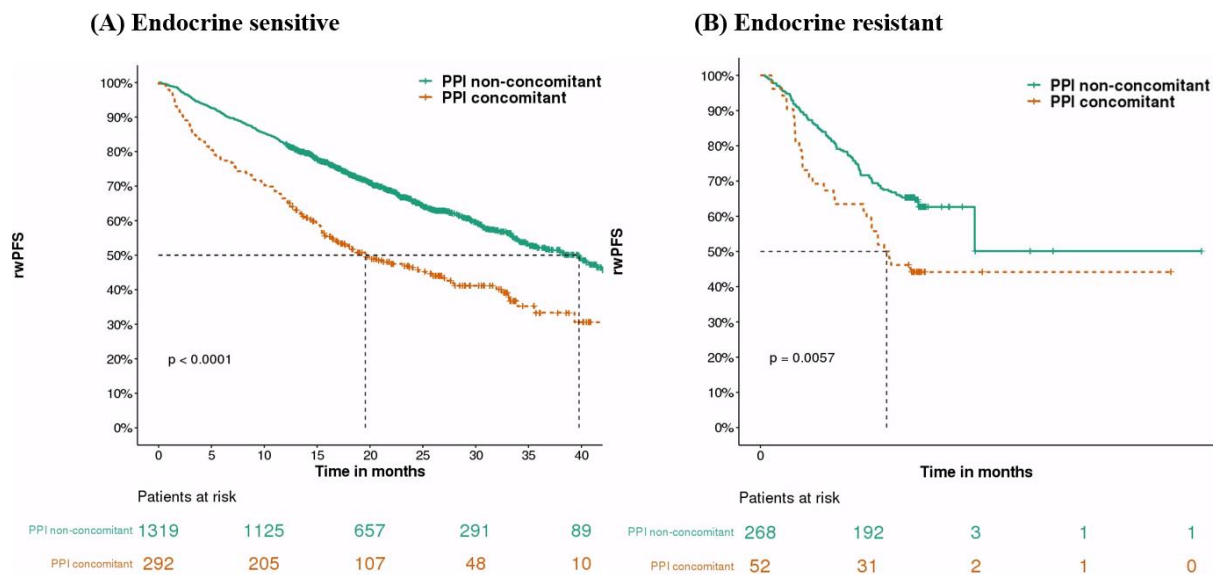
eFigure 6. Overall Survival in Patients With Endocrine-Sensitive and Endocrine-Resistant Treatment From 1:5 Matched Cohort

(A) Endocrine sensitive

p < 0.0001

Patients at risk

PPI non-concomitant	1319	1270	837	411	138
PPI concomitant	292	252	164	83	20

(B) Endocrine resistant

p = 0.0014

Patients at risk

PPI non-concomitant	268	242	4	1	0
PPI concomitant	52	40	1	1	0