REAL-WORLD EFFECTIVENESS OF PALBOCICLIB WITH CONCOMITANT PROTON PUMP INHIBITOR IN PATIENTS WITH BREAST CANCER IN SOUTH KOREA: A RETROSPECTIVE COHORT STUDY

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OBJECTIVES

- Palbociclib is a weak base medication whose absorption may be inhibited by concomitant proton pump inhibitors (PPIs).
- Although the clinical impact of concomitant use of PPI and palbociclib was evaluated in previous studies, a sufficient number of patients was not secured[1)2)].
- This study aims to identify the clinical impact of concomitant use of PPIs on palbociclib in patients with HER2-negative advanced breast cancer using nationwide claims data in South Korea.

METHODS

- In this retrospective cohort study, we identified patients with breast cancer taking palbociclib from November 1, 2017, to July 31, 2020 using Health Insurance Review & Assessment Service claims data.
- Those who co-administered PPIs for more than one-third of palbociclib treatment period were classified as PPI users, while those who did not take any PPIs in this period were classified as non-PPI users.
- We used propensity score matching (1:5) to minimize the impact of confounding factors such as age, menopause, metastasis, concomitant drug, and prior therapy.
- The index date of non-PPI users was matched to that of PPI users considering the duration between the date of the first prescription of palbociclib and the first PPI prescription. Both groups were followed after the index date until an event occurs or the end of the study period, July 31, 2021.
- Time to next treatment (TTNT) and overall survival (OS) were compared between the two groups. TTNT is a meaningful surrogate endpoint used as a proxy for progression-free survival. It was defined as the period from the index date to the initiation of a next line of treatment or death.
- We used the Kaplan-Meier method and log-rank test to compare the out comes between two groups. The adjusted hazard ratio (aHR) was estimated using a Cox proportional hazard model with covariates.
- Subgroup analysis was performed by classifying the patient groups according to the combined endocrine therapy (NSAI (non-steroidal aromatase inhibitor): 1st line; fulvestrant: subsequent line)

RESULTS

- Among 3,399 patients taking palbociclib, 344 and 1,587 patients were assigned to PPI and non-PPI groups, respectively, after matching.
- Of the PPI users , 291 patients were treated with NSAI and 53 patients were treated with fulvestrant (Table 1).

Table 1. Patient characteristics before and after matching

	Unmatched			Matched		
	PPI users	PPI non-users	SMD	PPI users	PPI non-users	SMD
All, n(%)	344(15)	2008(85)		344(100)	1587(100)	
Age group, n(%)			0.36			0.11
<50	53(15)	612(30)		53(15)	313(20)	
≥50	291(85)	1396(70)		291(85)	1274(80)	
Menopause, n(%)			-0.03			-0.03
Yes	338(98)	1981(99)		338(98)	1565(99)	
No	6(2)	27(1)		6(2)	22(1)	
Treatment combination, n(%)			-0.04			-0.05
palbociclib+NSAI (anastrozole/letrozole)	292(85)	1673(83)		292(85)	1319(83)	
palbociclib+fulvestrant	52(15)	335(17)		52(15)	268(17)	
CCI*, mean (std)	5.4(3.4)	4.7(3.4)	0.20	5.4 (3.4)	4.8 (3.4)	0.17
Prior chemotherapy, n(%)			-0.06			-0.03
Yes	4(1)	39(2)		4(1)	23(1)	
No	40(99)	1969(98)		340(99)	1564(99)	
Prior endocrine therapy, n(%)			0.00			-0.01
Yes	20(6)	116(6)		20(6)	95(6)	
No	324(94)	1892(94)		24(94)	492(94)	

- The median TTNT was significantly higher in PPI users compared to non-PPI users (18.1 months vs. 37.0 months, p-value < 0.0001).
- Non-PPI group had a superior TTNT benefit over PPI group (Figure 1) (Table 2).

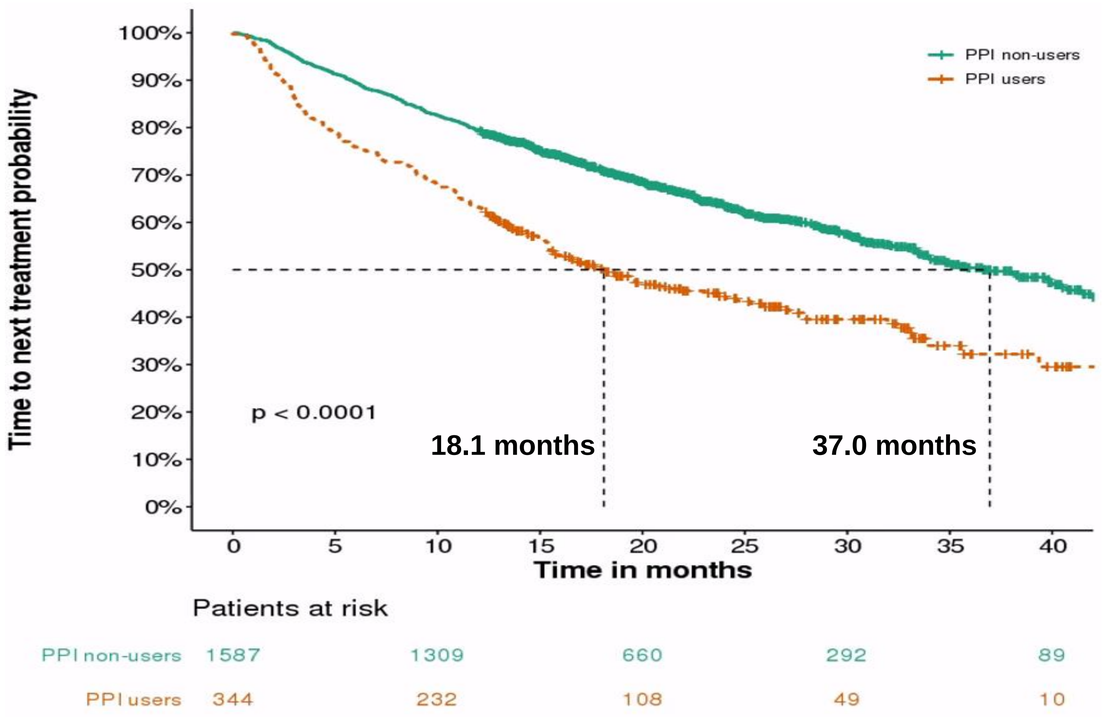

Figure 1. Time to next treatment in PPI and non-PPI groups

- The risk for OS was also significantly higher in the PPI group compared to non-PPI group (Figure 2) (Table 2).

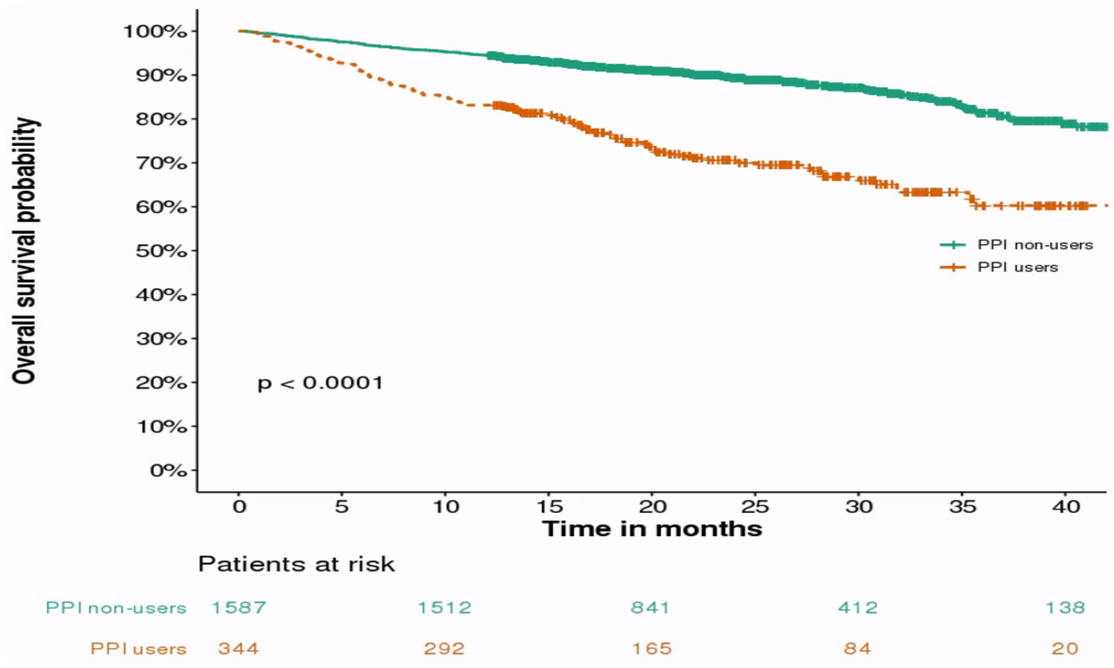

Figure 2. Overall survival in PPI and non-PPI groups

- The subgroup analysis also showed a stable results that the concomitant PPI increased the risk of TTNT and OS.(Table 2).

Table 2. Adjusted Hazard Ratio in PPI and non-PPI groups

	aHR (95% CI)	
	TTNT	OS
All	1.87 (1.59-2.20)	2.76 (2.16-3.52)
palbociclib+NSAI	1.89 (1.58-2.26)	2.79 (2.14-3.64)
Palbociclib+fulvestrant	1.79 (1.17-2.73)	3.07 (1.65-5.71)

CONCLUSIONS

- This real-world analysis found that concomitant use of PPI and palbociclib increase the risk of clinical outcomes compared to the palbociclib alone.
- For the maximum effect of palbociclib, PPI should be carefully prescribed in patients taking palbociclib.

REFERENCES

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