



From Trials to Practice: Exploring the Clinical Value of Potassium-competitive Acid Blockers

TO THE EDITOR: Proton pump inhibitors (PPIs) have been the mainstay of treatment of gastroesophageal reflux disease for over 3 decades. However, PPIs still exhibit limitations, such as a delayed onset of action and variable efficacy due to CYP2C19 polymorphisms, as well as the requirement for pre-meal dosing.¹ Potassium-competitive acid blockers (P-CABs) represent a new class of acid-suppressive agents that may address the limitations inherent to PPIs.¹ Since vonoprazan's introduction in 2015, 5 P-CABs are now available in 22 countries worldwide: vonoprazan (Dakeda, Japan, 2015), tegoprazan (HK Inno. N, South Korea, 2019), fexuprazan (Daewoong, South Korea, 2022), keverprazan (Carepher, China, 2023), and zastaprazan (Jeil, South Korea, 2024).² Their adoption has grown steadily, particularly in East Asia.

Although P-CABs have demonstrated pharmacologic advantages over PPIs,¹ their higher cost raises ongoing debate about whether they are truly necessary as a replacement for PPIs in clinical practice.³⁻⁶ We propose that this controversy stems, in part, from the limited scope of existing clinical studies, which have not convincingly demonstrated the proposed advantages of P-CABs. Most comparative studies between P-CABs and PPIs in gastroesophageal reflux disease have focused on mucosal healing and symptom improvement, generally showing non-inferiority rather than superiority.⁷⁻¹¹ Key patient-centered and practice-relevant parameters—such as dosing flexibility, time to symptom resolution, medication adherence, and health-related quality of life—are rarely assessed. Furthermore, the literature has largely overlooked the perspectives of prescribers. There is a paucity of data regarding physicians' clinical preferences, their perceptions of the value of P-CABs versus PPIs, and the clinical scenarios in which they prefer P-CABs, as well as whether they believe the additional cost is justified. As clinical experience with P-CABs continues to expand globally, we

believe there is a timely need for multicenter, real-world studies that address these underexplored dimensions.

We encourage future studies to evaluate the real-world effectiveness of P-CABs, including patient adherence, physician prescribing behaviors, and satisfaction with clinical outcomes in patients with typical, atypical, and refractory symptoms.^{12,13} Additionally, studies assessing both patient- and physician-reported outcomes, cost-effectiveness, and treatment satisfaction would provide a more comprehensive understanding of the clinical utility of P-CABs. Such evidence is essential not only for clinical decision-making but also for informing formulary policies and reimbursement strategies. We hope this letter will stimulate further research that reflects real-world use and integrates the perspectives of both patients and prescribers in assessing the role of P-CABs.

**Yong Sung Kim,^{1,8} Hyun Lim,^{2,8} Boram Cha,^{3,8} Seung Han Kim,^{4,8}
Da Hyun Jung,^{5,8} Su Jin Kim,^{6,8} and Suck Chei Choi^{7*}**

¹Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, Jeonlabuk-do, Korea; ²Department of Gastroenterology, Hallym University Sacred Heart Hospital, College of Medicine, Hallym University, Anyang, Gyeonggi-do, Korea; ³Department of Internal Medicine, College of Medicine, Inha University Hospital, Incheon, Korea; ⁴Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea; ⁵Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; ⁶Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Busan, Korea; ⁷Department of Gastroenterology, School of Medicine, Wonkwang University, Iksan, Korea; and ⁸Committee for International Cooperation, the Korean Society of Neurogastroenterology and Motility

1. Scarpignato C, Hunt RH. Potassium-competitive acid blockers: current clinical use and future developments. *Curr Gastroenterol Rep* 2024;26:273-293.
2. Yeom DH, Kim YS. History and pharmacological mechanism of gastric

- acid-suppressive drugs. *Korean J Helicobacter Up Gastrointest Res* 2023;23:159-166.
3. Patel A, Laine L, Moayyedi P, Wu J. AGA clinical practice update on integrating potassium-competitive acid blockers into clinical practice: expert review. *Gastroenterology* 2024;167:1228-1238.
 4. Habu Y, Hamasaki R, Maruo M, Nakagawa T, Aono Y, Hachimine D. Treatment strategies for reflux esophagitis including a potassium-competitive acid blocker: a cost-effectiveness analysis in Japan. *J Gen Fam Med* 2021;22:237-245.
 5. Kwon HY. So many choices, so little value: potential savings from selecting cost-effective proton pump inhibitors. *Pharmacoecon Open* 2025;9:461-469.
 6. Miwa H, Shiotani A, Takeda M, Eda M, Kato T, Yajima T. Health care cost analysis of PPI or P-CAB-first treatment in patients with gastro-esophageal reflux disease. *J Clin Gastroenterol* 2023;57:370-379.
 7. Ashida K, Sakurai Y, Hori T, et al. Randomised clinical trial: vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the healing of erosive oesophagitis. *Aliment Pharmacol Ther* 2016;43:240-251.
 8. Lee KJ, Son BK, Kim GH, et al. Randomised phase 3 trial: tegoprazan, a novel potassium-competitive acid blocker, vs. esomeprazole in patients with erosive oesophagitis. *Aliment Pharmacol Ther* 2019;49:864-872.
 9. Lee KN, Lee OY, Chun HJ, et al. Randomized controlled trial to evaluate the efficacy and safety of fexuprazan compared with esomeprazole in erosive esophagitis. *World J Gastroenterol* 2022;28:6294-6309.
 10. Chen S, Liu D, Chen H, et al. The efficacy and safety of keverprazan, a novel potassium-competitive acid blocker, in treating erosive oesophagitis: a phase III, randomised, double-blind multicentre study. *Aliment Pharmacol Ther* 2022;55:1524-1533.
 11. Oh JH, Kim HS, Cheung DY, et al. Randomized, double-blind, active-controlled phase 3 study to evaluate efficacy and safety of aastaprazan compared with esomeprazole in erosive esophagitis. *Am J Gastroenterol* 2025;120:353-361.
 12. Kim GH, Fass R. Potassium-competitive acid blockers for treatment of extraesophageal symptoms and signs. *J Neurogastroenterol Motil* 2025;31:170-177.
 13. Kim JE, Lee HJ, Kim MJ, Min YW, Rhee PL. Clinical characteristics of patients with proton pump inhibitor-refractory globus. *J Neurogastroenterol Motil* 2025;31:210-217.

Financial support: This work was supported by Wonkwang University 2025 (C.S.C.).

Conflicts of interest: None.

Author contributions: Yong Sung Kim: conceived and designed the study, and wrote the manuscript; Suck Chei Choi: conceived and designed the study and finally approved the manuscript; Hyun Lim, Boram Cha, Seung Han Kim, Da Hyun Jung, and Su Jin Kim, critically revised the manuscript. All authors approved the final version of the manuscript.
