Transl Clin Pharmacol. 2025 Dec;33(4):238-251
https://doi.org/10.12793/tcp.2025.33.e18
pISSN 2289-0882·eISSN 2383-5427

Translational and Clinical Pharmacology TCP

Original Article

Check for updates

Acid-suppressive effect of tegoprazan 12.5 mg BID: a phase 1 comparative study with tegoprazan 25 mg QD and famotidine 20 mg BID

Ho-Sook Kim [1], **Young-Kyung Choi** [1], **Minkyung Oh** [1], **Yong-Soon Cho** [1], and **Jong-Lyul Ghim** [2,*]

[1]Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan 47392, Korea
[2]Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan 47392, Korea

Received: Sep 30, 2025
Revised: Dec 3, 2025
Accepted: Dec 6, 2025
Published online: Dec 18, 2025

***Correspondence to**
Jong-Lyul Ghim
Department of Clinical Pharmacology, Inje University Busan Paik Hospital, 75 Bokji-ro, Busanjin-gu, Busan 47392, Korea.
Email: jonglyul.ghim@gmail.com

ORCID iDs
Ho-Sook Kim
https://orcid.org/0000-0001-6764-7261
Young-Kyung Choi
https://orcid.org/0000-0003-0931-9694
Minkyung Oh
https://orcid.org/0000-0001-7584-5436
Yong-Soon Cho
https://orcid.org/0000-0003-1424-1123
Jong-Lyul Ghim
https://orcid.org/0000-0002-6137-786X

Funding
This study was sponsored by HK inno.N Corp., Seoul, Republic of Korea.

Conflict of Interest
- Authors: Nothing to declare
- Reviewers: Nothing to declare
- Editors: Nothing to declare

ABSTRACT

Tegoprazan is a potassium-competitive acid blocker that directly inhibits the gastric proton pump, whereas famotidine is a histamine-2 receptor antagonist that indirectly suppresses acid secretion with known tolerance to repeated dosing. This phase 1 study evaluated the pharmacokinetics, pharmacodynamics, and safety of tegoprazan 12.5 mg twice daily (BID) compared with tegoprazan 25 mg once daily (QD) and famotidine 20 mg BID in healthy subjects. Thirty-six participants were randomized to one of the 3 regimens for 14 days. In pharmacokinetic analysis, tegoprazan 12.5 mg BID showed lower steady-state Cmax but higher trough concentrations than 25 mg QD, while overall systemic exposure was comparable, with a Day 14 geometric mean ratio for area under the concentration-time curve over 24 hours of 1.08 (90% confidence interval, 0.85–1.36). Pharmacodynamic assessment using 24-hour intragastric pH monitoring demonstrated superior and sustained acid suppression with tegoprazan 12.5 mg BID. On Day 14, the percentage of time with intragastric pH > 3 over 24 hours was 75.1% with tegoprazan 12.5 mg BID, compared with 55.4% with 25 mg QD and 40.3% with famotidine. Both tegoprazan regimens maintained relatively consistent acid suppression from Day 1 to Day 14 (71.8% to 75.1% and 56.4% to 55.4%), whereas famotidine showed a decline (65.3% to 40.3%). Similar time-dependent patterns were observed during the nighttime period and in the supine position. Tegoprazan 12.5 mg BID was well tolerated, with no adverse events reported in this group. These findings suggest that low-dose tegoprazan 12.5 mg BID provides safe and sustained acid suppression.

Keywords: Tegoprazan; Potassium-Competitive Acid Blocker; Drug Administration Schedule; Gastric Acidity Determination; Drug Tolerance

Reviewer
This article was reviewed by peer experts who are not TCP editors.

Author Contributions
Conceptualization: Kim HS, Ghim JL; Data curation: Choi YK; Formal analysis: Choi YK, Oh M; Investigation: Cho YS; Writing - original draft: Kim HS.

INTRODUCTION

Tegoprazan is a potassium-competitive acid blocker developed by HK inno.N to overcome the limitations of traditional proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs), such as delayed onset and inconsistent acid suppression. It provides rapid and sustained inhibition of gastric acid secretion. Tegoprazan 50 mg (K-CAB®) has been approved for the treatment of erosive and non-erosive gastroesophageal reflux disease (GERD), gastric ulcers, and as part of combination therapy for Helicobacter pylori eradication in patients with peptic ulcers or chronic atrophic gastritis [1-4].

A lower-dose formulation, tegoprazan 25 mg, was recently approved for maintenance therapy following treatment of erosive GERD and has demonstrated both safety and efficacy for up to 6 months of continuous use [5].

Acid-suppressive agents play an essential role not only in the treatment of acid-related gastrointestinal diseases but also in the prevention of upper gastrointestinal symptoms induced by medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and antiplatelet agents. With an aging population and the increasing prevalence of chronic conditions such as cardiovascular and musculoskeletal diseases, the use of NSAIDs and aspirin has risen. Given their associated risk of gastrointestinal injury, co-prescription of acid-suppressive agents is strongly recommended [6].

In such preventive strategies, PPIs are often prescribed at submaximal doses based on their dose-dependent acid-inhibitory effects. H2RAs, while less potent than PPIs in acid suppression, are widely used for intermittent or mild GERD, peptic ulcers, and gastritis due to their rapid onset, twice-daily dosing for prolonged effect, and cost-effectiveness.

H2RAs are particularly effective in suppressing nocturnal acid secretion, largely owing to their twice-daily regimen. Standard once-daily PPI therapy in the morning often fails to adequately control nighttime acid breakthrough, and the addition of an H2RA at bedtime has been shown to improve nocturnal acid suppression [7,8]. A meta-analysis of 8 randomized controlled trials demonstrated a reduction in the frequency of nocturnal acid breakthrough when a bedtime H2RA was added [9].

However, H2RAs are limited by the rapid development of tolerance with long-term use. For example, the acid-inhibitory effect of famotidine was shown to decrease after just 7 days of treatment [10]. In contrast, a previous study demonstrated that tegoprazan maintained its acid-suppressive effect over a 7-day period [11].

These findings suggest the potential value of low-dose tegoprazan regimens in the treatment or prevention of acid-related upper gastrointestinal symptoms, by overcoming the limitations of conventional PPIs and H2RAs while maintaining efficacy. Identifying the optimal dose and dosing schedule could enable effective symptom control with minimal adverse effects.

Therefore, in this phase 1 clinical trial, we aimed to evaluate the pharmacokinetics (PKs), pharmacodynamics (PDs), and safety of tegoprazan 12.5 mg administered twice daily (BID) compared with tegoprazan 25 mg once daily (QD) and famotidine 20 mg BID in healthy subjects. We further explored whether this dose could represent a minimally effective dose by comparing its acid-suppressive effects with those of tegoprazan 25 mg QD and famotidine 20 mg BID, with a particular focus on nocturnal acid suppression.

METHODS

Subjects

This study was reviewed and approved by the Institutional Review Board (IRB) of Inje University Busan Paik Hospital (IRB No. 2024-11-005) and authorized by the Korean Ministry of Food and Drug Safety. The trial adhered to the principles outlined in the Declaration of Helsinki and complied with the International Council for Harmonisation Good Clinical Practice guidelines. All volunteers were given a detailed explanation of the study procedures, potential risks, and expected benefits prior to participation, and written informed consent was obtained from each subject before any study-related activity.

Healthy volunteers between 19 and 45 years of age, with a body mass index (BMI) ranging from 18.5 to 28.0 kg/m^2, were considered eligible for inclusion.

Key exclusion criteria included a medical history or clinical evidence of dysfunction involving hepatic, renal, gastrointestinal, pulmonary, musculoskeletal, endocrine, psychiatric, hematologic-oncologic, urologic, or cardiovascular systems. Individuals with any condition that would interfere with pH catheter insertion, clinically significant abnormalities on baseline electrocardiogram (ECG), or laboratory findings exceeding the normal range were excluded. Specifically, subjects with alanine aminotransferase or aspartate aminotransferase levels > 1.5× the upper limit of normal (ULN), or total bilirubin > 2× ULN, were not eligible. Subjects who tested positive for H. pylori were also excluded, as chronic H. pylori infection may alter basal and stimulated gastric acid secretion and thereby confound the PD assessment.

Additional exclusion criteria included a positive result in a drug screening test, history of hypersensitivity to drugs, current or past substance abuse, use of medications known to influence the PKs of the investigational drug, intake of any medication within 10 days before screening, enrollment in another clinical trial within the past 6 months, or whole blood donation within 60 days prior to screening.

Subjects were also excluded if they failed to comply with medically acceptable contraception requirements, reported alcohol intake exceeding 30 g/day, smoked more than 10 cigarettes/day, or consumed over 400 mg/day of caffeine.

Study design

This was a randomized, open-label, multiple-dose, active-controlled, parallel-group study. A total of 36 healthy adult subjects were randomly assigned in a 1:1:1 ratio to one of the following 3 treatment groups: Group A (tegoprazan 12.5 mg BID), Group B (tegoprazan 25 mg QD), or Group C (famotidine 20 mg BID). All study medications were administered with 150 mL of water for 14 consecutive days, 30 minutes after the start of a standardized meal. As the morning and evening standardized meals were scheduled 12 hours apart, the twice-daily doses in Groups A and C were also administered 12 hours apart. Due to equipment limitations, subjects were admitted in 4 separate batches of 9 participants each. All participants were hospitalized for 16 nights and 17 days and completed a follow-up visit after discharge.

https://doi.org/10.12793/tcp.2025.33.e18

PK evaluation

PK blood samples were collected on Days 1 and 14 at multiple time points to characterize the concentration–time profile of tegoprazan and active metabolite M1. In Group A (12.5 mg BID), samples were obtained at 0 (pre-dose), 0.33, 0.66, 1, 1.5, 2, 3, 4, 8, 12, 12.33, 12.66, 13, 13.5, 14, 15, 16, 20, and 24 hours after the morning dose on Day 1, and at −12 and 0 (pre-dose), 0.33, 0.66, 1, 1.5, 2, 3, 4, 8, 12, 12.33, 12.66, 13, 13.5, 14, 15, 16, 20, and 24 hours on Day 14, capturing both dosing intervals.

In Group B (25 mg QD), samples were collected at 0 (pre-dose), 0.33, 0.66, 1, 1.5, 2, 3, 4, 8, 12, 16, and 24 hours on Day 1, and at −12 and 0 (pre-dose), 0.33, 0.66, 1, 1.5, 2, 3, 4, 8, 12, 16, and 24 hours on Day 14.

PK parameters were derived using non-compartmental methods implemented in Phoenix WinNonlin version 8.3 (Certara, Princeton, NJ, USA). On Day 1 Parameters included the maximum observed plasma concentration (C_{max}), time to reach C_{max} (T_{max}), area under the plasma concentration–time curve over 24 hours ($AUC_{0\text{-}24}$). For the 12.5 mg BID regimen, $AUC_{0–24}$ was calculated as the sum of the AUCs following the morning and evening doses. For C_{max} comparisons, the higher value between the morning and evening C_{max} was used as the representative C_{max}. On Day 14, PK parameters included maximum and minimum plasma concentrations at steady-state ($C_{max,ss}$ and $C_{min,ss}$), average plasma concentration at steady-state ($C_{avg,ss}$, calculated as $AUC_{0\text{-}24}$ on Day 14 divided by 24 hours).

Terminal elimination half-life ($t_{1/2β}$ on Day 1 and $t_{1/2β,ss}$ on Day 14) was calculated as ln(2)/$λ_z$, where $λ_z$ is the terminal elimination rate constant estimated by linear regression of the log-linear terminal phase following the morning dose in BID regimen. When $λ_z$ was based on fewer than 3 data points, the half-life was not estimated and reported as "Not Estimated." Observed accumulation index was calculated as the ratio of $AUC_{0\text{-}24}$ on Day 14 to that on Day 1, and fluctuation was computed as $(C_{max,ss} − C_{min,ss})/C_{avg,ss}$. Predicted accumulation index was derived from $λ_z$ using $1/(1 − e^{−λz·τ})$, with τ representing the dosing interval.

Bioanalysis

At each scheduled PK sampling point, 7 mL of venous blood was collected into EDTA K2 tubes using an intravenous catheter or syringe. The samples were stored in an ice bath immediately after collection and centrifuged within 30 minutes at 2,000 g for 10 minutes at 4°C. Plasma (0.5 mL) was aliquoted into cryovials and stored at −80°C until analysis. Plasma concentrations of tegoprazan and active metabolite, M1 were quantified using a validated liquid chromatography-tandem mass spectrometry method [12]. The bioanalysis was conducted by the bioanalytical team at BioInfra (Suwon, Korea). The precision and accuracy of the analytical method were confirmed based on the analysis of calibration standards and QC samples at 2.00, 6.00, 600, and 1,500 ng/mL, with all within-run and between-run relative standard deviation (SD) values ≤ 14.2% and percentage deviation of the mean from the theoretical concentration values within ± 13.5%, meeting the acceptance criteria of ≤ 15.0% (≤ 20.0% for lower limits of quantification).

PD evaluation

PD evaluation was performed using 24-hour intragastric pH monitoring with an ambulatory pH monitoring system (Digitrapper™ pH-Z, Medtronic, Minneapolis, MN, USA). The system was calibrated prior to use using standard pH 4.0 and 7.0 buffer solutions in accordance with the manufacturer's instructions and clinical practice guidelines [13]. A pH-sensitive catheter was transnasally inserted into the stomach, and pH recording was initiated simultaneously with the ingestion of 150 mL of water at the scheduled dosing time.

pH monitoring was conducted on Day −1 (baseline), and Days 1, 7, and 14. On each monitoring day, subjects remained in a seated position for 2 hours following drug administration, after which routine non-strenuous activities were permitted. Subjects maintained an upright posture (sitting or standing) at all times except during the designated supine period from 23:00 to 07:00. Daytime and nighttime were defined as 0–12 hours (08:00 to 20:00) and 12–24 hours (20:00 to 08:00), respectively.

To standardize physiological conditions, all participants remained fasting for 4 hours after drug administration on pH monitoring days; water was permitted after 2 hours. The same pre-dose water ingestion was replicated on Day −1 to mimic study drug administration conditions.

PD parameters included the mean and median intragastric pH over the 24-hour monitoring period; the percentage of time with pH above 3 ($T_{pH} > 3$) and above 4 ($T_{pH} > 4$); and the changes in these parameters from baseline (Δ mean pH, Δ median pH, $\Delta T_{pH} > 3$, and $\Delta T_{pH} > 4$).

Additional analyses were performed for daytime (08:00–20:00) and nighttime (20:00–08:00) intervals, as well as upright (08:00–23:00, 07:00–08:00) and supine (23:00–07:00) positions.

Safety evaluation

Safety was assessed throughout the study through adverse event (AE) monitoring, physical examinations, clinical laboratory tests, vital signs, and 12-lead ECGs conducted at scheduled intervals. All clinically relevant abnormalities were recorded as AEs. Each event was evaluated by the investigators for severity, seriousness, outcome, and its possible relationship to the study drug. AEs were coded by System Organ Class and Preferred Term, and their frequency and incidence were summarized by treatment group and severity. Drug-related AEs leading to discontinuation were specifically listed. Descriptive statistics were used to summarize changes in laboratory values, ECG findings, physical examination and vital signs from baseline across time points.

Statistical considerations

This study was exploratory in nature and was not based on formal power calculations. However, reference to prior studies suggested that a sample size of 10 subjects per group would be sufficient to detect a meaningful difference in the percentage of time with intragastric pH > 4 ($T_{pH} > 4$) between treatment arms. For example, after repeated administration for 7 days, tegoprazan 25 mg QD and famotidine 20 mg BID were previously reported to yield mean $T_{pH} > 4$ values of 56.6% (SD, 17.9) and 36.2% (SD, 8.7), respectively [10], corresponding to an estimated power of 85.3% at a 2-sided significance level of 0.05. Considering the exploratory objectives of the study and allowing for potential dropouts, a total of 36 participants (12 per treatment group) were planned for enrollment.

The PK parameters C_{max} and AUC_{0-24} were log-transformed and compared between treatment groups using analysis of variance (ANOVA) at a significance level of 0.05. A mixed-effects model was used, with treatment and separate hospitalization group (4 separate admission batches of 9 participants each) as fixed effects and subject as a random effect. Geometric mean ratios (GMRs) and their 90% confidence intervals were derived from this model as the ratio of the 12.5 mg BID group to the 25 mg QD group, with Group B serving as the reference. To assess steady-state attainment, trough (pre-dose) plasma concentrations at 12 hours on Day 13 and at 0, 12, and 24 hours on Day 14 in the BID group, and at 0 and 24 hours on Day 14 in the QD group, were analysed using a linear mixed-effects model with time as a fixed effect and subject as a random effect.

For PD analysis, differences in PD parameters between treatment groups (A vs. B, A vs. C, and B vs. C) were tested using either independent 2-sample t-tests or Mann–Whitney U tests, depending on data normality. Within-group comparisons across time points (Day 1 vs. Day 7, Day 1 vs. Day 14, and Day 7 vs. Day 14) were evaluated using paired t-tests or Wilcoxon signed-rank tests. To control for Type I error due to multiple comparisons, Bonferroni correction was applied, with statistical significance set at $\alpha = 0.0167$.

RESULTS

Subjects

All 36 participants who received at least one dose of the investigational product were male and were included in the safety analysis set. Among them, 24 subjects who completed all scheduled PK blood samplings per protocol were included in the PK analysis set. The PD analysis set comprised 34 subjects, excluding 2 individuals—one with improper pH catheter placement and another who did not complete the PD assessments. No participants had prior or concomitant medications that were expected to affect PK or PD outcomes.

The mean age was 26.8 ± 5.4 years in the 12.5 mg BID group, 28.9 ± 5.4 years in the 25 mg QD group, and 25.5 ± 2.9 years in the famotidine group. The corresponding mean body weights were 66.5 ± 9.1 kg, 71.0 ± 10.9 kg, and 68.0 ± 7.4 kg, respectively. The mean heights were 173.4 ± 6.0 cm, 173.4 ± 6.0 cm, and 172.1 ± 4.1 cm, and the mean BMI values were 22.0 ± 2.6 kg/m^2, 23.5 ± 2.8 kg/m^2, and 22.9 ± 2.2 kg/m^2, respectively, indicating comparable baseline demographic characteristics across the 3 treatment groups.

PKs

Steady-state attainment was confirmed in both treatment groups based on repeated trough concentration analysis. In the 12.5 mg twice-daily group, trough concentrations at 12 hours on Day 13 and at 0, 12, and 24 hours on Day 14 showed no significant differences over time based on a linear mixed-effects model, indicating achievement of steady state ($p = 0.112$). Similarly, in the 25 mg QD group, trough concentrations measured at 0 and 24 hours on Day 14 were comparable, confirming steady-state conditions ($p = 0.956$). On Day 14, the mean trough concentrations in the 12.5 mg BID group were notably higher than those in the 25 mg QD group (50.87 vs. 11.79 ng/mL at 0 hour and 51.37 vs. 11.74 ng/mL at 24 hours).

The mean plasma concentration–time profiles of tegoprazan and its active metabolite M1 are shown in **Fig. 1**, and the corresponding PK parameters are summarized in **Table 1**. Following single administration of tegoprazan 12.5 mg, C_{max} was reached at a median of 3.00 hours with a mean concentration of 99.98 ng/mL and eliminated with a mean $t_{1/2\beta}$ of 4.05 hours. After 14 days of repeated dosing, the morning dose yielded a C_{max} of 120.68 ng/mL (median T_{max} 4.00 hours) with a mean $t_{1/2\beta}$ of 4.52 hours. For the evening doses, C_{max} was 88.19 ng/mL (median T_{max} 2.99 hours, $t_{1/2\beta}$ 5.69 hours) on Day 1 and 108.68 ng/mL (median T_{max} 3.50 hours, $t_{1/2\beta}$ 6.71 hours) on Day 14, showing comparable trends to those observed for the morning doses.

Translational and Clinical Pharmacology TCP

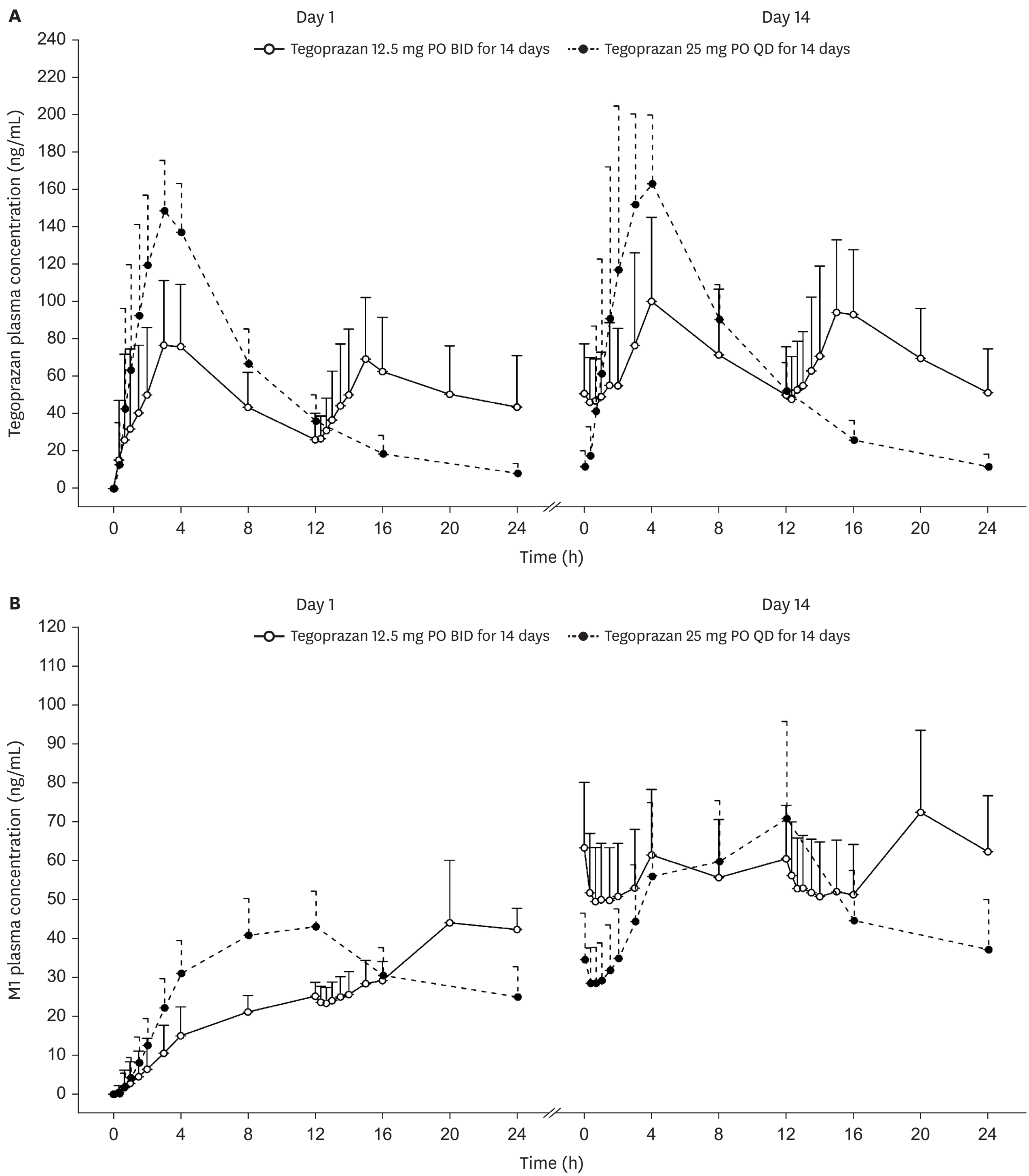

Figure 1. Mean plasma concentration—time profiles of tegoprazan (A) and its active metabolite M1 (B) following 14-day oral administration of tegoprazan 12.5 mg BID or 25 mg QD in healthy subjects. Data are expressed as mean ± standard deviation.
BID, twice daily; QD, once daily; PO, per os.

Table 1. Pharmacokinetic parameters of tegoprazan and its active metabolite M1 following single (Day 1) and multiple (Day 14) oral doses of tegoprazan 12.5 mg twice daily or 25 mg once daily

Parameters	Tegoprazan				M1			
	12.5 mg BID		25 mg QD		12.5 mg BID		25 mg QD	
	Day 1 (n = 12)	Day 14 (n = 12)	Day 1 (n = 12)	Day 14 (n = 12)	Day 1 (n = 12)	Day 14 (n = 12)	Day 1 (n = 12)	Day 14 (n = 12)
C_{max} (ng/mL)	99.98 ± 24.77	120.68 ± 30.47	151.33 ± 27.2	189.33 ± 47.96	25.93 ± 3.2	70.71 ± 15.89	43.98 ± 9.58	72.82 ± 24.45
$C_{min,ss}$ (ng/mL)	-	39.3 ± 21.66	-	10.67 ± 7.02	-	47.63 ± 13.32	-	27.48 ± 8.55
AUC_{0-24} (ng*h/mL)	1,185.59 ± 378.4	1,672.82 ± 599.93	1,221.01 ± 316.73	1,506.86 ± 377.51	609.84 ± 107.54	1,374.3 ± 311.34	729.79 ± 149.22	1,184.3 ± 322.62
T_{max} (h)	3 (0.66–8)	4 (1.5–11.98)	3 (1–4)	3 (1.5–8)	11.97 (4–11.98)	4 (0–11.97)	11.97 (8–11.97)	10.03 (4–12)
$t_{1/2\beta}$ (h)	4.05 ± 0.93	4.52 ± 2.06	4.71 ± 1.08	5 ± 0.92	NE	NE	12.59 ± 2.59	14.8 ± 4.06

Values are presented as mean ± standard deviation or median (range).
BID, twice daily; QD, once daily; C_{max}, maximum plasma concentration; $C_{min,ss}$, minimum plasma concentration at steady state; AUC_{0-24}, area under the plasma concentration–time curve over 24 hours; T_{max}, time to reach C_{max}; $t_{½β}$, terminal elimination half-life after the morning dose; NE, not estimated.

For the 25 mg once-daily group, C_{max} values after single and multiple dosing were 151.33 and 189.33 ng/mL, respectively, both with a median T_{max} of 3.00 hours and $t_{1/2\beta}$ values of 4.71 and 5.00 hours, respectively. The GMRs for AUC indicated comparable overall systemic exposure between the 12.5 mg BID and 25 mg QD regimens on both Day 1 and Day 14. In contrast, the C_{max} values with the 12.5 mg BID regimen were consistently higher than half of those observed with the 25 mg QD regimen (**Table 2**).

Although the per-dose amount of 12.5 mg BID is half that of 25 mg QD, the observed $C_{max,ss}$ values were approximately 67% of those in the QD group. This exceeds the expected 0.5 ratio based solely on dose, reflecting the influence of dosing frequency and drug accumulation. Because $C_{max,ss}$ is affected not only by dose but also by the dosing interval relative to the drug's half-life, a strictly proportional relationship should not be expected.

Observed accumulation indices were 1.40 for the 12.5 mg group and 1.24 for the 25 mg group. These exceeded the predicted indices of 1.00 and 1.03, respectively, but remained within the range defined as weak accumulation (1.2 ≤ AI < 2) and thus were not considered to indicate meaningful dose- and time-dependency [14].

The active metabolite M1 reached C_{max} at a median of 11.97 hours (mean 25.93 ng/mL) and 9.93 hours (49.38 ng/mL) after the morning and evening doses of 12.5 mg on Day 1, respectively. After repeated dosing, C_{max} increased to 70.71 ng/mL and 73.31 ng/mL, observed at 4.00 hours and 8.00 hours, respectively.

For the 25 mg group, M1 reached C_{max} at 11.97 hours (43.98 ng/mL) and 10.03 hours (72.82 ng/mL) after single and multiple dosing, with corresponding elimination half-lives of 12.59 hours and 14.80 hours [15].

Table 2. Geometric mean ratios and 90% CIs for pharmacokinetic parameters of tegoprazan (12.5 mg BID vs. 25 mg QD)

Parameters	Day	GMR (12.5 mg BID/25 mg QD)	90% CI
C_{max}	Day 1	0.68	0.58–0.79
	Day 14	0.67	0.57–0.80
AUC_{0-24}	Day 1	0.96	0.77–1.19
	Day 14	1.08	0.85–1.36

CI, confidence interval; BID, twice daily; QD, once daily; GMR, geometric mean ratio; C_{max}, maximum plasma concentration; AUC_{0-24}, area under the concentration–time curve over 24 hours.
AUC_{0-24} were obtained from a mixed-effects model with treatment and hospitalization batch as fixed effects and subject as a random effect. AUC values represent 24-hour exposure for both regimens.

Translational and Clinical Pharmacology TCP

PDs

PD parameters over 24 hours (0–24 hours), nighttime (20:00–08:00), and supine position (23:00–07:00) are summarized in **Table 3**, and the corresponding baseline-adjusted values are presented in **Table 4**.

Mean intragastric pH–time profiles after repeated dosing are shown in **Fig. 2**, demonstrating the temporal evolution of acid suppression across treatment groups. **Fig. 3** presents the mean (± SD) percentage of time with intragastric pH > 3 by treatment group, posture, and study day.

Over the 24-hour period on Day 14, the mean intragastric pH was 4.53 ± 0.79 in Group A, 3.80 ± 0.78 in Group B, and 3.04 ± 0.56 in Group C. The corresponding T_{pH} > 4 values were 64.32 ± 18.05%, 43.86 ± 19.11%, and 24.60 ± 14.07%, respectively, while T_{pH} > 3 values were 75.11 ± 15.56%, 55.38 ± 18.79%, and 40.29 ± 13.62%, respectively.

In pairwise comparisons over 24 hours, no statistically significant differences were observed between Groups A and B for mean pH, median pH, T_{pH} >3, or T_{pH} >4 at any time point. In contrast, comparisons between Groups B and C showed significant differences at Day 7 for T_{pH} >4 (p = 0.0109) and at Day 14 for both mean pH (p = 0.0149) and T_{pH} >4 (p = 0.0132). More pronounced differences were observed between Groups A and C, with mean pH, median pH, T_{pH} >3, and T_{pH} >4 all significantly different at both Day 7 and Day 14 (all $p \leq 0.0004$).

Table 3. Unadjusted pharmacodynamic parameters of intragastric pH following repeated doses of tegoprazan or famotidine in healthy subjects

Time period	Parameters	Day −1			Day 1			Day 7			Day 14		
		A (n = 12)	B (n = 10)	C (n = 12)	A (n = 12)	B (n = 10)	C (n = 12)	A (n = 12)	B (n = 10)	C (n = 12)	A (n = 12)	B (n = 10)	C (n = 12)
Over the 24-h period	Mean pH	2.78 ± 0.59	2.53 ± 0.38	2.62 ± 0.54	4.34 ± 0.84	3.91 ± 0.64	4.15 ± 0.73	4.57 ± 0.81	4.02 ± 0.81	3.29 ± 0.55	4.53 ± 0.79	3.8 ± 0.78	3.04 ± 0.56
	Median pH	2.48 ± 0.66	1.99 ± 0.37	2.16 ± 0.61	4.44 ± 1.13	3.72 ± 1.18	3.96 ± 1	4.78 ± 1.17	4.05 ± 1.42	2.93 ± 0.79	4.76 ± 1.13	3.53 ± 1.28	2.65 ± 0.77
	T_{pH} > 3 (%)	33.94 ± 19.11	26.44 ± 12.34	29.23 ± 14.16	71.81 ± 20.27	56.44 ± 13.85	65.26 ± 15.43	73.36 ± 17.52	61.82 ± 17.02	45.09 ± 14.64	75.11 ± 15.56	55.38 ± 18.79	40.29 ± 13.62
	T_{pH} > 4 (%)	20.67 ± 15.79	16.33 ± 9.8	17.23 ± 13.44	57.72 ± 22.35	45.91 ± 17.59	49.06 ± 18.85	63.67 ± 20.56	51.41 ± 18.55	31.44 ± 14.85	64.32 ± 18.05	43.86 ± 19.11	24.6 ± 14.07
Supine position	Mean pH	2.18 ± 0.64	1.73 ± 0.09	1.98 ± 0.52	3.88 ± 0.86	2.46 ± 0.38	4.38 ± 0.98	4.01 ± 0.8	3.04 ± 0.88	3.48 ± 0.79	4.04 ± 0.8	2.81 ± 0.76	2.91 ± 0.74
	Median pH	1.91 ± 0.45	1.7 ± 0.08	1.76 ± 0.22	3.56 ± 1.25	2.13 ± 0.2	4.13 ± 1.69	3.82 ± 1.42	2.54 ± 0.78	3.12 ± 1.49	3.95 ± 1.1	2.53 ± 0.89	2.33 ± 0.66
	T_{pH} > 3 (%)	12.88 ± 18.24	0.24 ± 0.51	7.08 ± 11.86	58.22 ± 25.2	15.84 ± 11.17	59.9 ± 17.91	57.58 ± 20.9	32.75 ± 21.19	40.69 ± 19.66	64.87 ± 19.25	25.34 ± 21.41	29.02 ± 19.31
	T_{pH} > 4 (%)	9.84 ± 15.1	0.1 ± 0.25	4.61 ± 8.98	44.12 ± 25.08	8.59 ± 9.2	49.78 ± 21.7	45.53 ± 19.1	24.33 ± 19.5	35.23 ± 17.82	49.31 ± 20.69	15.97 ± 15.45	22.12 ± 16.17
Night time	Mean pH	2.62 ± 0.67	2.21 ± 0.3	2.42 ± 0.56	4.17 ± 0.85	3.19 ± 0.51	4.29 ± 0.83	4.32 ± 0.75	3.53 ± 0.81	3.44 ± 0.72	4.39 ± 0.78	3.26 ± 0.76	3.05 ± 0.72
	Median pH	2.18 ± 0.78	1.76 ± 0.1	1.93 ± 0.38	4.18 ± 1.28	2.4 ± 0.52	4.02 ± 1.16	4.44 ± 1.33	3.29 ± 1.31	3.08 ± 1.11	4.59 ± 1.05	2.8 ± 1.06	2.58 ± 0.79
	T_{pH} > 3 (%)	26.28 ± 20.16	15.51 ± 8.21	21.14 ± 13.53	66.25 ± 23.12	35.21 ± 11.49	64.58 ± 14.75	66.22 ± 17.53	47.19 ± 17.42	43.14 ± 18.55	72.57 ± 17.03	40.46 ± 20.54	36.32 ± 18.4
	T_{pH} > 4 (%)	18.09 ± 17.8	10.28 ± 8.27	13.38 ± 12.64	52.11 ± 23.23	27.04 ± 13.63	49.48 ± 19.63	54.76 ± 18.04	36.87 ± 18.34	33.69 ± 17.44	59.6 ± 18.29	30.11 ± 17.65	24.31 ± 16.55

Values are presented as mean ± standard deviation.
A: tegoprazan 12.5 mg BID; B: tegoprazan 25 mg QD; C: famotidine 20 mg BID; Day −1: baseline (prior to first dosing); Mean pH: arithmetic mean of continuously measured intragastric pH over the specified period; Median pH: median of intragastric pH values over the period; T_{pH} > 3 or > 4: proportion of time during each period in which intragastric pH exceeded 3 or 4, respectively; Over the 24-hour period: 08:00–08:00 the next day; Nighttime: 20:00–08:00; Supine position: 23:00–07:00.
BID, twice daily; QD, once daily.

Translational and Clinical Pharmacology TCP

Table 4. Baseline-adjusted pharmacodynamic parameters of intragastric ph following repeated doses of tegoprazan or famotidine in healthy subjects

Time period	Parameters	Day 1			Day 7			Day 14		
		A (n = 12)	B (n = 10)	C (n = 12)	A (n = 12)	B (n = 10)	C (n = 12)	A (n = 12)	B (n = 10)	C (n = 12)
Over the 24-h period	ΔMean pH	1.56 ± 0.61	1.38 ± 0.47	1.54 ± 0.4	1.79 ± 0.63	1.5 ± 0.64	0.67 ± 0.34	1.75 ± 0.57	1.27 ± 0.73	0.42 ± 0.36
	ΔMedian pH	1.95 ± 0.86	1.73 ± 1.04	1.8 ± 0.65	2.3 ± 0.97	2.06 ± 1.25	0.78 ± 0.48	2.27 ± 1.02	1.54 ± 1.17	0.5 ± 0.5
	ΔT_{pH} >3 (%)	37.86 ± 18.73	30 ± 8.02	36.04 ± 8.35	39.42 ± 18.39	35.38 ± 12.04	15.86 ± 7.57	41.17 ± 13.28	28.94 ± 16.73	11.06 ± 9.59
	ΔT_{pH} >4 (%)	37.06 ± 18.08	29.58 ± 13.75	31.83 ± 11.86	43 ± 16.91	35.08 ± 14.68	14.21 ± 8.41	43.65 ± 14.16	27.53 ± 16.97	7.38 ± 8.98
Supine position	ΔMean pH	1.7 ± 0.83	0.73 ± 0.35	2.4 ± 0.63	1.82 ± 0.88	1.31 ± 0.88	1.5 ± 0.77	1.85 ± 0.62	1.08 ± 0.74	0.93 ± 0.66
	ΔMedian pH	1.64 ± 1.09	0.42 ± 0.17	2.37 ± 1.59	1.91 ± 1.39	0.83 ± 0.76	1.36 ± 1.47	2.03 ± 0.96	0.83 ± 0.88	0.57 ± 0.64
	ΔT_{pH} >3 (%)	45.34 ± 28.71	15.6 ± 10.96	52.82 ± 14.11	44.7 ± 25.09	32.51 ± 21.03	33.62 ± 19.5	51.99 ± 18.29	25.1 ± 21.37	21.95 ± 18.25
	ΔT_{pH} >4 (%)	34.28 ± 27.07	8.49 ± 9.12	45.16 ± 16.84	35.69 ± 20.35	24.23 ± 19.45	30.61 ± 16.81	39.47 ± 15.12	15.86 ± 15.47	17.51 ± 13.95
Night time	ΔMean pH	1.55 ± 0.67	0.98 ± 0.41	1.87 ± 0.47	1.7 ± 0.72	1.32 ± 0.77	1.02 ± 0.57	1.77 ± 0.53	1.05 ± 0.71	0.63 ± 0.52
	ΔMedian pH	2 ± 1.05	0.64 ± 0.48	2.09 ± 0.94	2.26 ± 1.24	1.53 ± 1.31	1.16 ± 0.9	2.41 ± 0.84	1.04 ± 1.05	0.65 ± 0.56
	ΔT_{pH} >3 (%)	39.96 ± 23.79	19.7 ± 7.16	43.43 ± 9.21	39.94 ± 21.29	31.68 ± 16.83	21.99 ± 15.25	46.29 ± 17.05	24.95 ± 19.94	15.18 ± 13.69
	ΔT_{pH} >4 (%)	34.02 ± 22.4	16.76 ± 11.09	36.1 ± 12.99	36.67 ± 17.81	26.59 ± 17.76	20.32 ± 12.36	41.52 ± 13.65	19.82 ± 16.34	10.94 ± 10.18

Values are presented as mean ± standard deviation.
A: tegoprazan 12.5 mg BID; B: tegoprazan 25 mg QD; C: famotidine 20 mg BID; Day −1: baseline (prior to first dosing); ΔMean pH: change in arithmetic mean of continuously measured intragastric pH from baseline; ΔMedian pH: change in median intragastric pH from baseline; ΔT_{pH} > 3 or > 4: change in the percentage of time with intragastric pH above 3 or 4, respectively, from baseline; Over the 24-hour period: 08:00–08:00 the next day; Nighttime: 20:00–08:00; Supine position: 23:00–07:00.
BID, twice daily; QD, once daily.

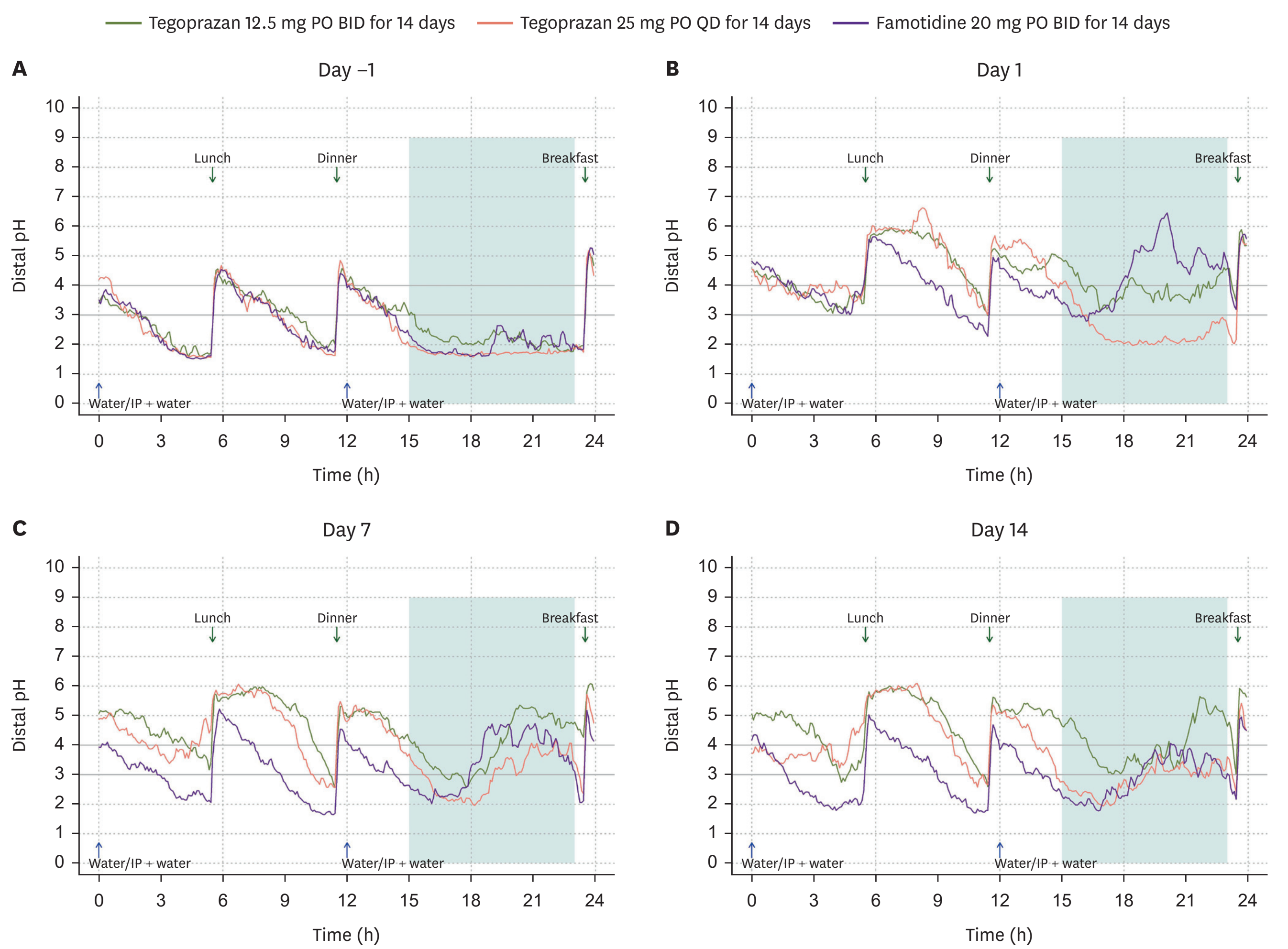

Figure 2. Mean 24-hour intragastric pH–time profiles following repeated oral administration of tegoprazan 12.5 mg BID, 25 mg QD, or famotidine 20 mg BID on Day −1 (baseline, A), Day 1 (B), Day 7 (C), and Day 14 (D) in healthy subjects. Data represent mean distal intragastric pH values over time. Meals and scheduled water intake are marked with green and blue arrows, respectively. The shaded area indicates the nighttime (23:00–07:00).
BID, twice daily; QD, once daily; PO, per os.

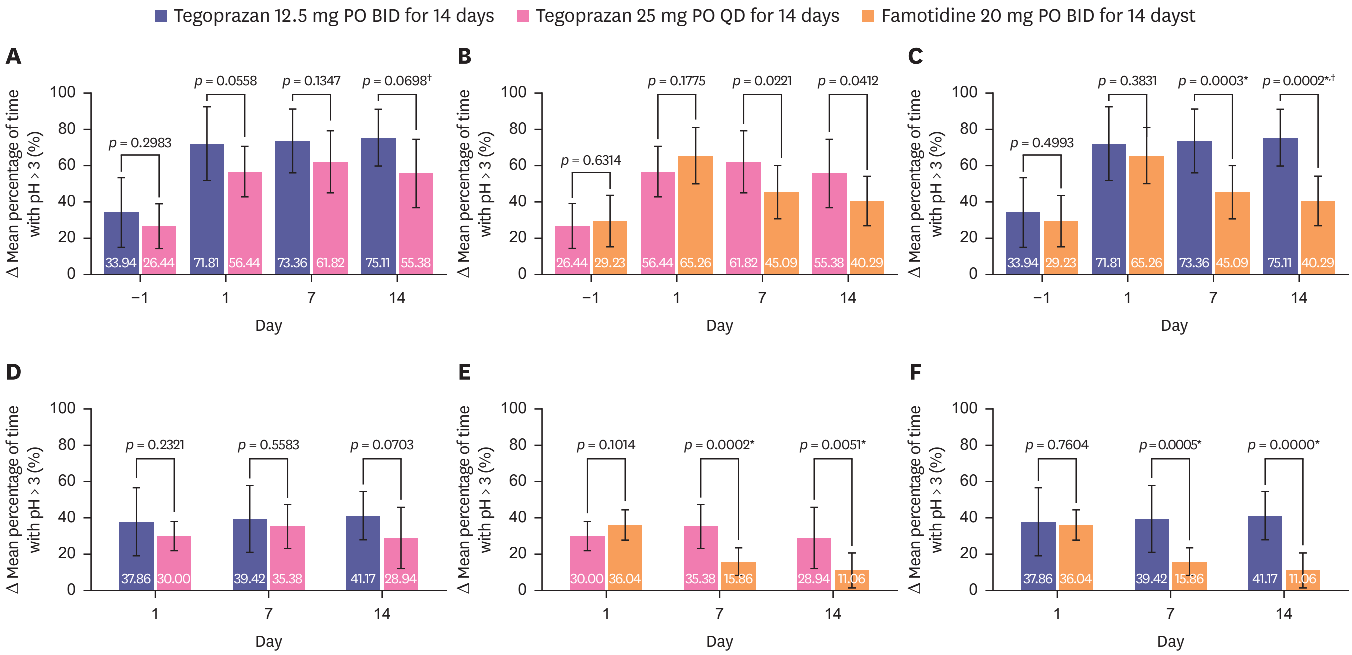

Figure 3. Comparative analysis of the percentage of time with intragastric pH > 3 (A-C) and Δpercentage of time with pH > 3 from baseline (D-F) over the 24-hour period following 14-day oral administration of tegoprazan 12.5 mg BID, 25 mg QD, or famotidine 20 mg BID in healthy subjects. Panels (A, D) show comparisons between tegoprazan 12.5 mg BID and 25 mg QD; (B, E) between tegoprazan 25 mg QD and famotidine 20 mg BID; and (C, F) between tegoprazan 12.5 mg BID and famotidine 20 mg BID. Data are presented as mean ± standard deviation. Statistical comparisons were performed using independent 2-sample *t*-tests or Mann–Whitney *U* tests.
BID, twice daily; QD, once daily; PO, per os.
*$p < 0.0167$ after Bonferroni correction; †Not significant.

Baseline-adjusted analyses showed consistent findings. At Day 14, Δmean pH was 1.75 ± 0.57 in Group A, 1.27 ± 0.73 in Group B, and 0.42 ± 0.36 in Group C, with corresponding $\Delta T_{pH} > 4$ values of 43.65 ± 14.16%, 27.53 ± 16.97%, and 7.38 ± 8.98%. Baseline-adjusted $\Delta T_{pH} > 3$ and $\Delta T_{pH} > 4$ differed significantly between Groups B and C and between Groups A and C at both Day 7 and Day 14 (all $p \leq 0.0051$), whereas no significant differences were observed between Groups A and B at any time point.

These findings demonstrate that acid suppression with famotidine declined significantly over time, while both tegoprazan regimens maintained stable efficacy from Day 7 to Day 14.

During the nighttime period, at Day 14, Group A maintained a higher mean pH (4.39 ± 0.78) and greater $T_{pH} > 4$ (59.60 ± 18.29%) than Group B (3.26 ± 0.76 and 30.11 ± 17.65%) and Group C (3.05 ± 0.72 and 24.31 ± 16.55%). Baseline-adjusted nighttime $\Delta T_{pH} > 4$ at Day 14 was 41.52 ± 13.65% in Group A, compared with 19.82 ± 16.34% in Group B and 10.94 ± 10.18% in Group C.

Pairwise testing confirmed that Group A differed significantly from Group C for nighttime mean pH, $T_{pH} > 3$, and $T_{pH} > 4$ at both Day 7 and Day 14 (all $p \leq 0.0083$), and significant differences between Groups A and B were also observed for multiple nighttime parameters at Day 14 ($p \leq 0.0141$).

In the supine position, at Day 14, mean pH was 4.04 ± 0.80 in Group A versus 2.81 ± 0.76 in Group B and 2.91 ± 0.74 in Group C. Baseline-adjusted $\Delta T_{pH} > 4$ values were 39.47 ± 15.12%, 15.86 ± 15.47%, and 17.51 ± 13.95%, respectively.

Pairwise comparisons showed that Group A was significantly superior to Group C for all key PD parameters (mean pH, T_{pH} > 3, T_{pH} > 4, Δmean pH, ΔT_{pH} > 3, and ΔT_{pH} > 4) at Day 14 in the supine position (all $p \leq 0.0018$). Differences between Groups A and B were also significant for several supine parameters at Day 14 ($p \leq 0.0148$).

Taken together, the superiority of tegoprazan over famotidine—across T_{pH} > 3 and T_{pH} > 4, baseline-adjusted parameters, postural conditions, and nighttime periods—was consistently evident from Day 7 and maintained through Day 14, whereas famotidine showed a clear time-dependent attenuation of acid-suppressive effect.

Safety

Tegoprazan was well tolerated in healthy subjects. A total of 3 AEs were reported: 2 events of diarrhea in 2 subjects in the tegoprazan 25 mg QD group and one event of urticaria in one subject in the famotidine 20 mg BID group. All AEs were mild in severity and judged as possibly related to the study drug. No unexpected adverse drug reactions were observed. There were no serious adverse events, study discontinuations, or study drug withdrawals due to AEs during the study period. Furthermore, no clinically significant changes from baseline were observed in physical examinations, clinical laboratory tests, vital signs, or 12-lead ECGs.

DISCUSSION

In this study, the PKs, PD, and safety profiles of tegoprazan 12.5 mg administered BID, tegoprazan 25 mg QD, and famotidine 20 mg BID were evaluated in healthy subjects following oral administration for 14 days after meals.

The 2 tegoprazan regimens showed comparable systemic exposure based on AUC, with the 12.5 mg BID regimen exhibiting higher trough concentrations and peak concentrations that exceeded the expected 0.5 ratio derived from dose reduction. The GMR of steady-state C_{max} was approximately 0.7, reflecting this observation. These findings suggest that dosing frequency and accumulation contribute meaningfully to systemic exposure, beyond the linearity of dose alone. However, systemic exposure (AUC) was comparable between groups, with GMRs close to 1.0, indicating similar overall drug exposure upon repeated dosing.

From a PD standpoint, famotidine 20 mg BID initially provided rapid acid suppression, but a well-known tachyphylaxis effect reduced its efficacy over time. On Day 1, the degree of gastric acid suppression was comparable to that observed with tegoprazan. However, a progressive loss of PD effect was observed from Day 7 onward, with further attenuation by Day 14, consistent with previous findings. In contrast, tegoprazan 12.5 mg BID maintained stable and sustained efficacy through Day 14, without evidence of tachyphylaxis. These differences were particularly evident in baseline-adjusted outcomes, including mean pH and percentage of time with intragastric pH > 3 or 4, where famotidine showed minimal improvement while both tegoprazan regimens demonstrated clear and persistent effects.

This time-dependent attenuation with famotidine was clearly demonstrated by a significant reduction in 24-hour T_{pH} > 3 from 65.3% on Day 1 to 45.1% on Day 7 and further to 40.3% on Day 14. In contrast, both tegoprazan regimens showed no comparable time-dependent attenuation, maintaining relatively stable 24-hour acid control over the same period (12.5 mg BID: from 71.8% to 75.1%; 25 mg QD: from 56.4% to 55.4%). These between-group differences were statistically significant after adjustment for multiple comparisons, underscoring the clinical relevance of sustained acid suppression with tegoprazan.

These findings are of clinical relevance, as nighttime gastric acid breakthrough is a common contributor to reflux-related symptoms and sleep disturbance. Importantly, superior acid-suppressive effect of tegoprazan over famotidine was demonstrated from Day 7 and maintained through Day 14 across all postural and temporal conditions.

Unlike H_2-receptor antagonists, which act on upstream histamine receptors and are prone to receptor-level tolerance with repeated use [14,15], tegoprazan acts directly and reversibly on the final effector of acid secretion—the H^+/K^+-ATPase [14,16]. This mechanism minimizes receptor desensitization or upregulation effects and explains the sustained acid-suppressive efficacy observed over 14 days without evidence of tachyphylaxis [15,16].

Although no statistically significant differences were observed in the overall 24-hour PD parameters between the 2 tegoprazan regimens, a consistent numerical advantage was observed for the 12.5 mg BID regimen over the 25 mg QD regimen, particularly during the nighttime and supine periods. On Day 14, these differences reached statistical significance across multiple endpoints, highlighting the potential benefit of split dosing even at the lowest approved dose. These results align with prior findings that twice-daily dosing of acid-suppressive therapy may offer enhanced nocturnal acid control [17].

Tegoprazan 12.5 mg BID was well tolerated in this study. No AEs were reported in this group, while 3 mild, drug-related AEs occurred in the other treatment groups and resolved without intervention. In addition, no clinically significant changes were observed in physical examinations, vital signs, laboratory tests, or ECGs. However, the limited sample size and short study duration restrict the generalizability of the safety findings. Furthermore, although famotidine 20 mg BID served as an active control, dose equivalence between this regimen and tegoprazan was not formally established, which may limit direct quantitative comparisons.

Although multiplicity correction was applied, the exploratory nature of the study still imposes limitations on statistical inference. Thus, these findings should be interpreted with caution and considered hypothesis-generating. Nonetheless, the consistent and durable acid-suppressive effects observed with tegoprazan 12.5 mg BID—particularly during clinically relevant nocturnal periods—underscore its potential as an effective therapeutic option. Further confirmatory studies in patient populations are warranted to evaluate the clinical utility of split dosing and its role in optimizing the management of acid-related disorders.

ACKNOWLEDGMENTS

This manuscript's English expression was refined with the assistance of ChatGPT-4o (OpenAI, San Francisco, CA, USA), and the final responsibility for the content rests entirely with the authors.

The authors thank the staff of the Clinical Trials Center of Inje University Busan Paik for their generous cooperation.

REFERENCES

1. Kim SH, Cho KB, Chun HJ, Lee SW, Kwon JG, Lee DH, et al. Randomised clinical trial: comparison of tegoprazan and placebo in non-erosive reflux disease. Aliment Pharmacol Ther 2021;54:402-411. PUBMED | CROSSREF
2. Cho YK, Choi MG, Choi SC, Lee KM, Kim TO, Park SH, et al. Randomised clinical trial: tegoprazan, a novel potassium-competitive acid blocker, or lansoprazole in the treatment of gastric ulcer. Aliment Pharmacol Ther 2020;52:789-797. PUBMED | CROSSREF
3. Lee KJ, Son BK, Kim GH, Jung HK, Jung HY, Chung IK, 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. PUBMED | CROSSREF
4. Choi YJ, Lee YC, Kim JM, Kim JI, Moon JS, Lim YJ, et al. Triple therapy-based on tegoprazan, a new potassium-competitive acid blocker, for first-line treatment of *Helicobacter pylori* infection: a randomized, double-blind, phase III, clinical trial. Gut Liver 2022;16:535-546. PUBMED | CROSSREF
5. Cho YK, Kim JH, Kim HS, Kim TO, Oh JH, Choi SC, et al. Randomised clinical trial: comparison of tegoprazan and lansoprazole as maintenance therapy for healed mild erosive oesophagitis. Aliment Pharmacol Ther 2023;57:72-80. PUBMED | CROSSREF
6. Joo MK, Park CH, Kim JS, Park JM, Ahn JY, Lee BE, et al. Clinical guidelines for drug-induced peptic ulcer, 2020 revised edition. Korean J Gastroenterol 2020;76:108-133. PUBMED | CROSSREF
7. Mainie I, Tutuian R, Castell DO. Addition of a H2 receptor antagonist to PPI improves acid control and decreases nocturnal acid breakthrough. J Clin Gastroenterol 2008;42:676-679. PUBMED | CROSSREF
8. Zacny J, Zamakhshary M, Sketris I, Veldhuyzen van Zanten S. Systematic review: the efficacy of intermittent and on-demand therapy with histamine H2-receptor antagonists or proton pump inhibitors for gastro-oesophageal reflux disease patients. Aliment Pharmacol Ther 2005;21:1299-1312. PUBMED | CROSSREF
9. Wang Y, Pan T, Wang Q, Guo Z. Additional bedtime H2-receptor antagonist for the control of nocturnal gastric acid breakthrough. Cochrane Database Syst Rev 2009;2009:CD004275. PUBMED | CROSSREF
10. Shimatani T, Inoue M, Kuroiwa T, Moriwaki M, Xu J, Ikawa K, et al. Which has superior acid-suppressive effect, 10 mg omeprazole once daily or 20 mg famotidine twice daily?: effects of single or repeated administration in japanese-negative CYP2C19 extensive metabolizers. Dig Dis Sci 2007;52:390-395. PUBMED | CROSSREF
11. Han S, Choi HY, Kim YH, Nam JY, Kim B, Song GS, et al. Randomised clinical trial: safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple oral doses of tegoprazan (CJ-12420), a novel potassium-competitive acid blocker, in healthy male subjects. Aliment Pharmacol Ther 2019;50:751-759. PUBMED | CROSSREF
12. Guo K, He X, Zhao H, Ma C. Characterisation of degradation products of tegoprazan by LC-MS and GC-MS. J Pharm Biomed Anal 2023;228:115323. PUBMED | CROSSREF
13. Trudgill NJ, Sifrim D, Sweis R, Fullard M, Basu K, McCord M, et al. British Society of Gastroenterology guidelines for oesophageal manometry and oesophageal reflux monitoring. Gut 2019;68:1731-1750. PUBMED | CROSSREF
14. Shin JM, Sachs G. Pharmacology of proton pump inhibitors. Curr Gastroenterol Rep 2008;10:528-534. PUBMED | CROSSREF
15. Inatomi N, Matsukawa J, Sakurai Y, Otake K. Potassium-competitive acid blockers: advanced therapeutic option for acid-related diseases. Pharmacol Ther 2016;168:12-22. PUBMED | CROSSREF
16. Hori Y, Matsukawa J, Takeuchi T, Nishida H, Kajino M, Inatomi N. A study comparing the antisecretory effect of TAK-438, a novel potassium-competitive acid blocker, with lansoprazole in animals. J Pharmacol Exp Ther 2011;337:797-804. PUBMED | CROSSREF
17. Bowser JJ, Houston-Harris JL, Shepler BM, Stewart CF. Splitting PPI doses improves nocturnal acid suppression. Ann Pharmacother 1998;32:1179-1183.

https://doi.org/10.12793/tcp.2025.33.e18