Gut and Liver
https://doi.org/10.5009/gnl230242
pISSN 1976-2283 eISSN 2005-1212

Original Article

The Effect of Tegoprazan on the Treatment of Endoscopic Resection-Induced Artificial Ulcers: A Multicenter, Randomized, Active-Controlled Study

Byung-Wook Kim[1], Jong Jae Park[2], Hee Seok Moon[3], Wan Sik Lee[4], Ki-Nam Shim[5], Gwang Ho Baik[6], Yun Jeong Lim[7], Hang Lak Lee[8], Young Hoon Youn[9], Jun Chul Park[10], In-Kyung Sung[11], Hyunsoo Chung[12], Jeong Seop Moon[13], Gwang Ha Kim[14], Su Jin Hong[15], Hyuk Soon Choi[16]

[1]Department of Internal Medicine, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea; [2]Division of Gastroenterology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea; [3]Department of Internal Medicine, Chungnam National University College of Medicine, Daejeon, Korea; [4]Department of Internal Medicine, Chonnam National University Hwasun Hospital, Hwasun, Korea; [5]Department of Internal Medicine, Ewha Womans University College of Medicine, Seoul, Korea; [6]Department of Internal Medicine, Hallym University Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea; [7]Department of Internal Medicine, Dongguk University Ilsan Hospital, Dongguk University College of Medicine, Goyang, Korea; [8]Department of Internal Medicine, Hanyang University Medical Center, Seoul, Korea; [9]Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; [10]Department of Gastroenterology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; [11]Department of Internal Medicine, Konkuk University Medical Center, Konkuk University College of Medicine, Seoul, Korea; [12]Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; [13]Department of Internal Medicine, Inje University Seoul Paik Hospital, Inje University College of Medicine, Seoul, Korea; [14]Department of Internal Medicine, Pusan National University College of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan, Korea; [15]Digestive Disease Center and Research Institute, Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea; [16]Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Article Info

Received June 25, 2023
Revised August 18, 2023
Accepted August 22, 2023
Published online February 22, 2024

Corresponding Author

Jong Jae Park
ORCID https://orcid.org/0000-0002-4642-5405
E-mail gi7pjj@korea.ac.kr

Background/Aims: Tegoprazan is a novel potassium-competitive acid blocker that has beneficial effects on acid-related disorders such as gastroesophageal reflux and peptic ulcer diseases. This study aimed to validate the effect of tegoprazan on endoscopic submucosal dissection (ESD)-induced artificial ulcers.

Methods: Patients from 16 centers in Korea who underwent ESD for gastric neoplasia were enrolled. After ESD, pantoprazole was administered intravenously for 48 hours. The patients were randomly allocated to either the tegoprazan or esomeprazole group. Tegoprazan 50 mg or esomeprazole 40 mg were administered for 4 weeks, after which gastroscopic evaluation was performed. If the artificial ulcer had not healed, the same dose of tegoprazan or esomeprazole was administered for an additional 4 weeks, and a gastroscopic evaluation was performed.

Results: One hundred sixty patients were enrolled in this study. The healing rates of artificial ulcers at 4 weeks were 30.3% (23/76) and 22.1% (15/68) in the tegoprazan and esomeprazole groups, respectively (p=0.006). At 8 weeks after ESD, the cumulative ulcer healing rates were 73.7% (56/76) and 77.9% (53/68) in the tegoprazan and esomeprazole groups, respectively (p=0.210). Delayed bleeding occurred in two patients in the tegoprazan group (2.6%) and in one patient in the esomeprazole group (1.5%). Other adverse events were negligible in both groups.

Conclusions: Tegoprazan showed similar effects on post-ESD artificial ulcer healing in comparison with esomeprazole. **(Gut Liver 2024;18:257-264)**

Key Words: Tegoprazan; Endoscopic resection; Endoscopic submucosal dissection; Gastric neoplasia; Multicenter prospective randomized study

INTRODUCTION

Acid-reducing agents, such as proton pump inhibitors (PPIs), are administered after endoscopic submucosal dissection (ESD) for gastric neoplasia and non-ampullary duodenal tumors to avoid adverse events such as delayed bleeding.[1-3] PPIs should be administered before meal; however, approximately half the patients do not take PPIs before breakfast,[4] thus limiting their effects. Potassium-competitive acid blockers (P-CABs), which are novel acid-reducing agents, have been introduced to overcome the limitations of PPIs. P-CABs can be taken regardless of the meal times.

Vonoprazan, one of the P-CABs developed in Japan, has shown some benefits over PPIs in *Helicobacter pylori* eradication and the treatment of peptic ulcer diseases and gastroesophageal reflux diseases.[5-7] Vonoprazan was also as effective as PPIs in preventing bleeding after ESD and healing of artificial ulcers after ESD for gastric neoplasia.[8,9] Tegoprazan is a novel P-CAB developed in Korea that suppresses gastric acid secretion faster and more potently than PPIs.[10] It is as effective as PPIs in the treatment of gastric ulcers and in *H. pylori* eradication.[11,12] Tegoprazan is also effective in the treatment of gastroesophageal reflux diseases.[13,14] However, the effect of tegoprazan in healing artificial ulcers after ESD is yet to be elucidated. This study aimed to evaluate the efficacy and safety of tegoprazan in the treatment of artificial ulcers after ESD in comparison to those of PPIs.

MATERIALS AND METHODS

1. Study design and data management

This study was a multicenter, randomized, double-blind, active-controlled, non-inferiority trial comparing tegoprazan (50 mg/day) and esomeprazole (40 mg/day). The study protocol was approved by the Korean Ministry of Food and Drug Safety (Registration number 32524) and the institutional review boards of each institution including Korea University Guro Hospital (IRB number: 2020GR0069). This study followed the Declaration of Helsinki and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use-Good Clinical Practice guidelines. Informed consent was obtained from all patients prior to enrollment. This study was registered at the Korean Disease Control and Prevention Agency registration site, Clinical Research Information Service (KCT0005470).

Drug distribution was determined according to the drug randomization number generated by an interactive web response system (cubeIWRS; CRScube Inc., Seoul, Korea). A double-dummy method, using matching tegoprazan 50 mg and esomeprazole 40 mg, was employed to ensure that the study was double-blinded with key codes kept off-site by an external data manager. All medications were provided in sealed boxes and supplied by the medication supervisor to ensure blinded allocation. Blinded data were securely stored and could only be accessed by authorized personnel. All authors had access to the study data and reviewed and approved the final manuscript.

2. Patients

This study was performed at 16 centers in Korea. Inclusion criteria were as follows: patients aged 20 to 75 years who were diagnosed histologically and endoscopically with (1) gastric adenoma; (2) differentiated type gastric adenocarcinoma without ulcer; (3) differentiated type gastric adenocarcinoma with ulcer not involving submucosa less than 3.0 cm; (4) differentiated type gastric adenocarcinoma infiltrating submucosa less than 500 μm without ulcer less than 3.0 cm; and (5) undifferentiated type gastric adenocarcinoma not involving the submucosa without ulcer less than 2.0 cm. Exclusion criteria were as follows: (1) the size of artificial ulcer after ESD was over 4.0 cm; (2) overt bleeding or perforation after ESD; (3) past history of upper gastrointestinal tract surgery; (4) esophageal stricture, gastric outlet obstruction, or active peptic ulcer; (5) follow-up gastroscopy not available; (6) past history of adverse events to tegoprazan, PPI, or benzimidazole; (7) patients who were taking atazanavir, nelfinavir, rilpivirine, terfenadine, cisapride, pimozide, or astemizole; (8) pregnant or nursing women; (9) patients with uncontrolled cardiopulmonary diseases, renal diseases, liver diseases, neurologic diseases, or endocrine diseases including diabetes; (10) patients with cognition disorder or mental retardation; (11) patients who were taking anti-depressants, anxiolytics, or anti-psychotics; (12) patients who took PPI or H_2 receptor antagonists within 2 weeks before ESD; (13) patients who were taking steroids, nonsteroidal anti-inflammatory drugs, aspirin, anti-platelet agents, or anticoagulants during the study period; (14) patients with aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, or bilirubin over 2 times the reference value; or (15) patients with blood urea nitrogen or creatinine over 1.5 times the reference value. Fasting serum gastrin level was checked on day zero and 4 and 8 weeks after ESD.

3. Endoscopic submucosal dissection

ESD was performed under conscious sedation. Sedative drugs were chosen by each endoscopist's preference. A mixture of 0.001% epinephrine, 0.1% indigo carmine,

and normal saline was injected into submucosal layer and mucosal cutting followed by submucosal dissection was performed using each endoscopist's preference of knives. Hemorrhage during the procedure was controlled with hemostatic forceps. After ESD, the size of artificial ulcer was measured using biopsy forceps.

4. Administration of tegoprazan or esomeprazole

Immediately after ESD, a bolus of 80 mg pantoprazole was administered intravenously, followed by 8 mg per hour for 48 hours. Eligible patients were randomly assigned in a 1:1 ratio to receive either tegoprazan or esomeprazole during this period. Two days after ESD, the patients were instructed to take one tablet of 50 mg tegoprazan with one placebo esomeprazole tablet (tegoprazan group) or one placebo tegoprazan tablet with one tablet of 40 mg esomeprazole (esomeprazole group) once daily before breakfast for 4 weeks. Gastroscopic evaluation was performed 4 weeks after ESD. When an artificial ulcer was found in the active or healing stage according to Sakita-Miwa's classification on gastroscopy 4 weeks after ESD, 50 mg tegoprazan with placebo or 40 mg esomeprazole with placebo was administered 4 weeks more. In these patients, gastroscopic evaluation was performed again 8 weeks after ESD. The study process is illustrated in Fig. 1.

5. Outcomes

The primary endpoint of this study was the healing rates of ESD-induced artificial ulcers at 4 and 8 weeks. The secondary endpoints were as follows: (1) healing rates of ESD-induced artificial ulcers at 4 weeks and 8 weeks; (2) change in ulcer size; and (3) the incidence of delayed bleeding. Healing of ESD-induced artificial ulcer was defined as the complete closure of the mucosal defect. The ulcer size was measured as follows: the mucosal defect after ESD was considered elliptical, and the area was calculated by multiplying the long axis radius and the short axis radius, followed by multiplying π, and expressed in mm^2. The shrinkage rates of the artificial ulcers at 4 and 8 weeks were also compared as an exploratory endpoint. The shrinkage rate of artificial ulcers was calculated as the ratio of ulcer size at 4 and 8 weeks to the ulcer size immediately after ESD. The size of the artificial ulcer was measured using opening biopsy forceps. Delayed bleeding was defined by overt hemorrhage signs such as hematemesis or melena over 24 hours after initiating either tegoprazan or esomeprazole along with a decrease in hemoglobin level of over 2.0 g/dL.

Safety was evaluated using vital signs (blood pressure, heart rate, and body temperature), physical examination, serum gastrin level, and incidence of treatment-emergent adverse events (TEAEs). A TEAE was defined as an adverse event that occurred after the participant received the study drug. TEAEs were categorized by severity and relativity and compared between the treatment groups. Adverse events were analyzed in the safety set.

6. Statistical analysis

For sample size calculation, the healing rate of artificial ulcers at 8 weeks was assumed to be 95.5% for tegoprazan and esomeprazole, with a non-inferiority margin of –10% and a power of 80% at a significant level of 2.5% (one-sided).[15] While a direct comparison between vonoprazan and tegoprazan for artificial ulcer healing is lacking, an indirect

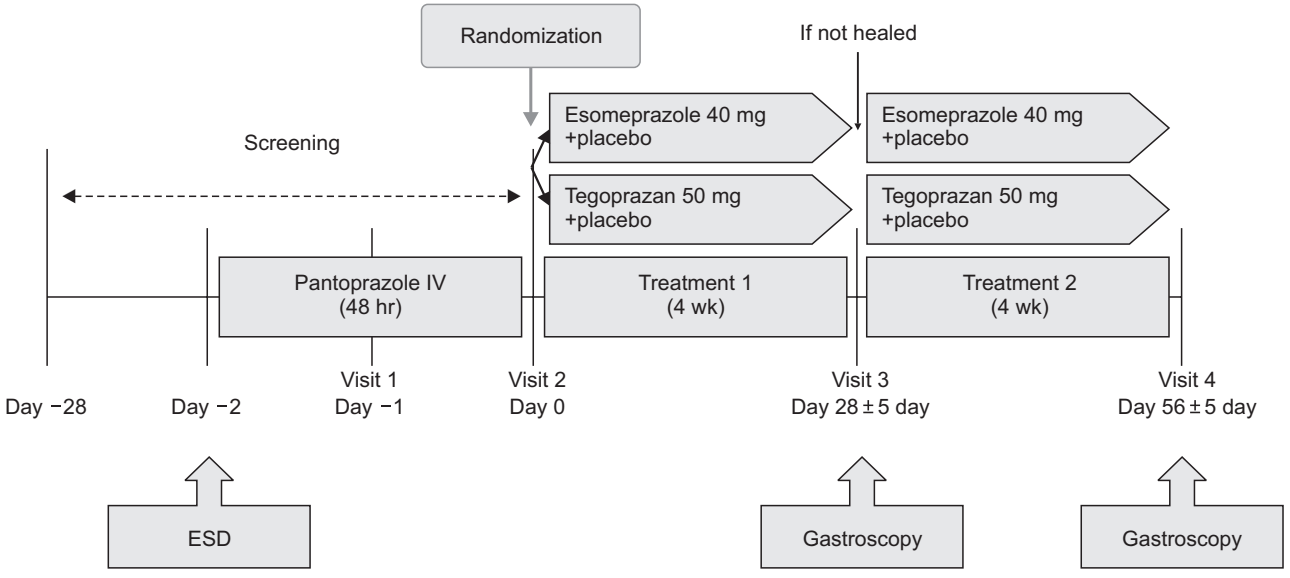

Fig. 1. A diagram indicating the progression of the study. IV, intravenous; ESD, endoscopic submucosal dissection.

comparison was conducted using data from reports. Specifically, it was found that vonoprazan exhibited comparable effectiveness to lansoprazole in healing gastric ulcers (93.5% for vonoprazan and 93.8% for lansoprazole), and similarly, tegoprazan demonstrated comparable efficacy to lansoprazole in gastric ulcer healing (95.0% for tegoprazan and 95.7% for lansoprazole).[6,11] The total sample size was 160 subjects, with 80 patients per treatment group, considering a 15% drop-out.

For continuous variables, the values are provided as the number of subjects, mean, standard deviation, median, minimum and maximum. For categorical variables, the values are presented as frequencies and percentages. The non-inferiority test of tegoprazan versus esomeprazole in healing rate was to be declared if the lower bound of the two-sided 95% confidence interval for the difference between the two arms was greater than the non-inferiority margin, –10%. Continuous variables were compared by the Student t-test or Wilcoxon rank-sum test depending on whether the normality assumption was satisfied. Categorical variables were compared by the chi-square test or Fisher exact test depending on whether 20% or more of cells with an expected frequency of 5 or less were found.

All two-sided statistical tests were performed at a significance level of 5% unless otherwise specified. Statistical analyses were performed using SAS 9.4 (SAS Institution Inc., Cary, NC, USA).

RESULTS

1. Baseline characteristics

Among the 167 patients with an artificial ulcer after ESD who were screened, three were ineligible based on the inclusion/exclusion criteria, and four withdrew their consent. These participants were considered to have screening failure, and the remaining 160 patients were randomized in a 1:1 ratio to one of the two treatment arms: tegoprazan or esomeprazole. Among the 160 randomized patients, 16 (10.0%) were discontinued from the study due to the lack of viable data (n=10, 6.3%), violation of an inclusion/exclusion criteria (n=5, 3.1%), or withdrawal of consent before exposure to the study drug (n=1, 0.6%) (Fig. 2). The baseline characteristics of the patients are summarized in Table 1. No significant differences in baseline characteristics were observed between the treatment groups.

2. Ulcer healing

The healing rates of artificial ulcers at 4 weeks were 30.3% (23/76) and 22.1% (15/68) in tegoprazan group and in esomeprazole group, respectively. The percentage difference between the tegoprazan group and esomeprazole group was <–10% (95% confidence interval, –6.07 to 22.48), which confirmed the non-inferiority of the tegoprazan group in comparison to the esomeprazole group. At 8 weeks after ESD, the cumulative healing rates of artificial ulcers were 73.7% (56/76) and 77.9% (53/68) in tegoprazan

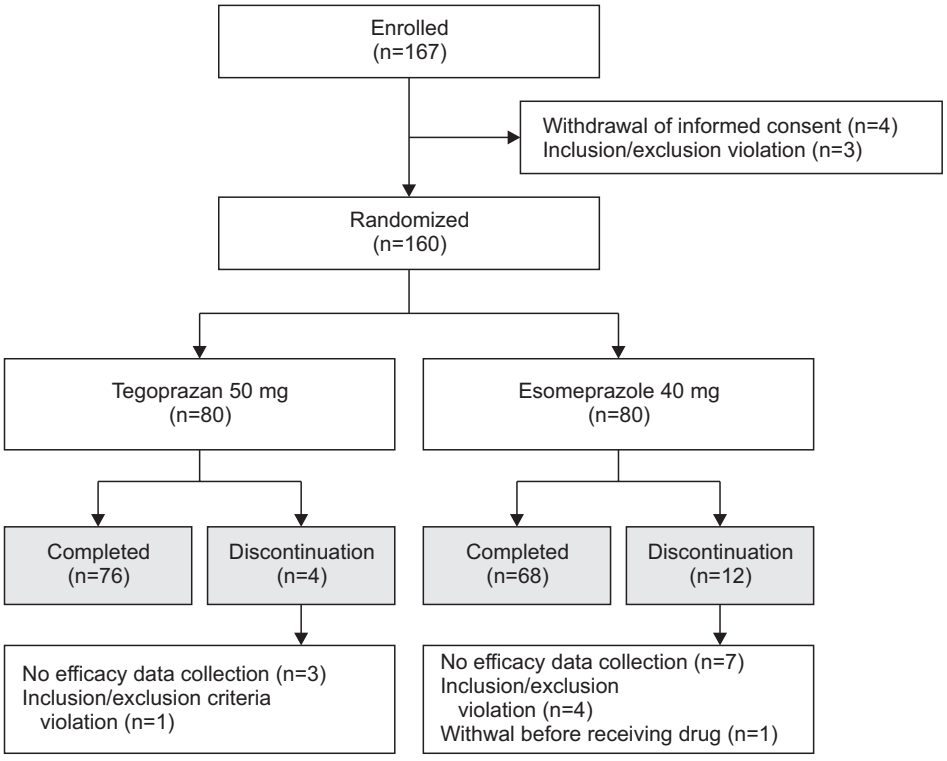

Fig. 2. Disposition of patients included in this study.

and esomeprazole groups, respectively (95% confidence interval, –18.23 to 9.71). The results are summarized in Table 2. Immediately after ESD, the ulcer size was 508.18±274.10 mm^2 and 585.63±309.72 mm^2 in tegoprazan group and esomeprazole groups, respectively (p=0.180). Four weeks after ESD, the ulcer size was 51.63±75.06 mm^2 and 60.26±79.51 mm^2 in tegoprazan and esomeprazole groups, respectively (p=0.400). Eight weeks after ESD, the ulcer size was 2.64±7.93 mm^2 and 8.19±41.68 mm^2 in tegoprazan and esomeprazole groups, respectively (p=0.761). The two groups showed no difference in changes in ulcer stages. A summary of the changes in ulcer stages can be found in Table 3.

At 4 weeks after ESD, the shrinkage rates of artificial ulcers were 85.6% in tegoprazan group and 85.0% in esomeprazole group, respectively (p=0.897). At 8 weeks after ESD, the shrinkage rates of artificial ulcers were 94.9% and 94.2% in the tegoprazan and esomeprazole groups, respectively (p=0.842).

3. Delayed bleeding and safety

Delayed bleeding occurred in two patients (2.6%) from the tegoprazan group and in one patient (1.5%) from the esomeprazole group (p=1.000). In all cases, melena was the first sign of delayed bleeding. One patient from the tegoprazan group experienced melena 9 days after ESD, and another patient from the same group had melena 14 days after ESD. One patient from the esomeprazole group had melena 10 days after ESD. Gastroscopy confirmed bleeding from the ESD site, with Forrest Ib observed in one patient from the esomeprazole group and Forrest IIa in two patients from the tegoprazan group. Delayed bleeding was successfully managed using endoscopic hemostasis in all the patients. Hemoglobin levels dropped from 2.1 g/dL to 3.2 g/dL.

Safety analysis was performed in 159 patients who received ≥1 dose of the study drug and underwent ≥1 safety assessment in this clinical trial. Among the 159 patients, 15 cases of TEAEs were reported in 12 patients. In the esomeprazole group only, one nausea, urticarial, and skin rash were reported as drug-related TEAEs (n=1, 1.28%).

4. Serum gastrin level

The baseline serum gastrin levels were 94.99±105.78 pg/mL and 100.81±119.89 pg/mL for the tegoprazan and esomeprazole groups, respectively (Fig. 3). The serum gastrin levels were 82.14±70.5 pg/mL and 86.52±72.57 pg/mL at 4 weeks and 99.22±86.24 pg/mL and 96.21±81.65 pg/mL at 8 weeks for the tegoprazan and esomeprazole groups, re-

Table 1. Baseline Characteristic of Patients in the Full Analysis Set

Characteristic	Tegoprazan group (n=76)	Esomeprazole group (n=68)
Sex, No. (%)		
Male	57 (75.0)	46 (67.7)
Female	19 (25.0)	22 (32.3)
Age, mean±SD, yr	62.0±7.4	63.0±7.8
Social history, No. (%)		
Smoking	16 (21.1)	9 (13.2)
Alcohol	29 (38.2)	18 (26.5)
Pre-procedural histology, No. (%)		
Adenoma, low grade dysplasia	41 (54.0)	37 (54.4)
Adenoma, high grade dysplasia	13 (17.1)	13 (19.1)
Differentiated adenocarcinoma	17 (22.4)	17 (25.0)
Undifferentiated adenocarcinoma	2 (2.6)	1 (1.5)
Mixed	3 (4.0)	0
Ulcer size immediately after ESD, mean±SD, mm^2	507.1±277.7	562.9±324.8

ESD, endoscopic submucosal dissection.

Table 3. Changes in Ulcer Stages at 4 and 8 Weeks after ESD

	Tegoprazan group (n=74)	Esomeprazole group (n=67)
4 wk after ESD		
A1/A2	8 (10.8)	10 (14.9)
H1/H2	43 (58.1)	42 (62.7)
S1/S2	23 (31.1)	15 (22.4)
8 wk after ESD		
A1/A2	1 (1.4)	2 (3.0)
H1/H2	17 (23.0)	12 (17.9)
S1/S2	56 (75.7)	53 (79.1)

Data are presented as number (%).
ESD, endoscopic submucosal dissection.

Table 2. Cumulative Healing Rates of Artificial Ulcers

Variable	Healing of the artificial ulcer (%)	Difference, % (95% CI)	p-value
4 wk		8.20 (–6.07 to 22.48)	0.006
Tegoprazan group	30.3 (23/76)		
Esomeprazole group	22.1 (15/68)		
8 wk		–4.20 (–18.23 to 9.71)	0.210
Tegoprazan group	73.7 (56/76)		
Esomeprazole group	77.9 (53/68)		

Data are presented as percentages with number of subjects in parentheses, confidence interval (CI), non-inferiority margin –10%.

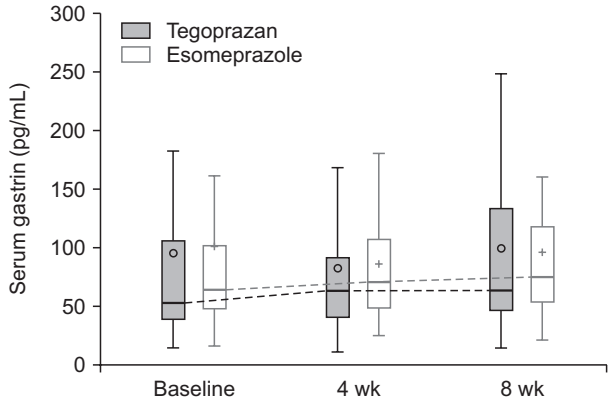

Fig. 3. Changes in the serum gastrin level before and after tegoprazan and esomeprazole administration.

spectively. The changes in serum gastrin levels did not differ significantly between the tegoprazan and esomeprazole groups.

DISCUSSION

In this study, we found that 50 mg of tegoprazan was not inferior to 40 mg of esomeprazole in treating artificial ulcers after ESD for gastric neoplasia. The healing rate of artificial ulcers at 4 weeks after ESD was higher in the tegoprazan group than in the esomeprazole group, whereas cumulative healing rate at 8 weeks after ESD did not show a significant difference between the two groups. From these results, it is plausible that tegoprazan has a more potent acid-suppressive effect than esomeprazole; therefore, the healing process after ESD progressed rapidly in the tegoprazan group. Some studies have observed that vonoprazan, another P-CAB, was superior to PPIs in the healing of artificial ulcers after ESD for gastric neoplasia, indicating similarities with our study.[9,16] However, it is still uncertain whether P-CAB is superior to PPI in the healing of artificial ulcers after ESD for gastric neoplasia. A systematic review and meta-analysis showed that vonoprazan was superior to PPI at 4 weeks after ESD,[17] whereas another recent systematic review and meta-analysis showed that there was no difference between vonoprazan and PPI.[18]

The healing rate of artificial ulcers at 4 weeks after administration of P-CABs or PPIs was reported to range from less than 10% to over 90% in various studies.[16,19,20] This large variation among the studies might result from interpretation of H_3 stage ulcers according to the Sakita-Miwa classification.[21] In this study, the healing rates of artificial ulcers were 30.3% in the tegoprazan group and 22.1% in the esomeprazole group at 4 weeks after ESD. This result was similar to a recent study comparing the efficacy of vonoprazan and lansoprazole treatment for artificial ulcers.[19] We strictly interpreted the ulcer stages and even minute ulcer bases were classified as healing stages. Additionally, the shrinkage rates of artificial ulcers should not be misinterpreted as complete healing. At 8 weeks after ESD, the artificial ulcers healed by more than 70% in both groups in this study. Considering these results, acid-reducing agents should be administered at least 8 weeks after ESD. Since cumulative ulcer healing rates at 8 weeks after ESD were not 100% in both groups, an adequate duration of acid-reducing agents used after ESD for gastric neoplasia should be elucidated in further studies.

Our study did not show any difference in delayed bleeding rates between the tegoprazan and esomeprazole groups. Delayed bleeding was not the main outcome of our study, and the number of patients enrolled in this study might not have been sufficient. Considering that most delayed bleeding occurs within a week after ESD,[22] delayed bleeding may be preventable with more potent acid suppression. A large-scale prospective study is needed to elucidate the effect of tegoprazan on delayed bleeding.

Although P-CABs can overcome some of the unmet needs of PPIs, they still have some limitations in clinical practice. It is well known that serum gastrin levels might increase after administration of P-CABs.[23] Tegoprazan has a different chemical structure than vonoprazan and revaprazan. There were no changes in the serum gastrin levels in either group in this study. This was similar to the results of previous studies.[11,24] Therefore, tegoprazan might be safely administered for up to 8 weeks. Further studies with large numbers of patients are warranted.

The strength of this study is that it is a multicenter, randomized, double-blind, active-controlled study. Despite this strength, this is a non-inferiority study, and it cannot be concluded that 50 mg of tegoprazan is superior to 40 mg of esomeprazole in the healing of artificial ulcers after ESD for gastric neoplasia. Another limitation is that intravenous pantoprazole was administered for 48 hours before starting oral tegoprazan or esomeprazole because tegoprazan cannot be administered intravenously. Therefore, the immediate effect of tegoprazan after ESD was not evaluated in this study. Hemoglobin levels were not checked within 2 weeks after ESD, which may lead to underestimation of delayed bleeding occurrences.

In conclusion, this is the first study to investigate the effect of tegoprazan on the healing of artificial ulcers after ESD for gastric neoplasia. Tegoprazan showed a similar effect on post-ESD artificial ulcer healing in comparison to esomeprazole, constituting that tegoprazan can be a new option for the treatment of ESD-induced artificial ulcers.

CONFLICTS OF INTEREST

This study was supported by HK Inno.N Corp. HK Inno.N provided financial support and study drug. However, no role in the design of this study, study conduct, data analysis, and interpretation of the data.

B.W.K. and G.H.K. are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

ACKNOWLEDGEMENTS

This study was supported by HK Inno.N Corp. HK Inno.N provided financial support and study drug.

AUTHOR CONTRIBUTIONS

Study concept and design: J.J.P. Data acquisition: B.W.K., J.J.P., H.S.M., W.S.L., K.N.S., G.H.B., Y.J.L., H.L.L., Y.H.Y., J.C.P., I.K.S., H.C., J.S.M., G.H.K., S.J.H., H.S.C. Data analysis and interpretation: B.W.K. Drafting of the manuscript: B.W.K. Critical revision of the manuscript for important intellectual content: J.J.P., H.S.M., W.S.L., K.N.S., G.H.B., Y.J.L., H.L.L., Y.H.Y., J.C.P., I.K.S., H.C., J.S.M., G.H.K., S.J.H., H.S.C. Statistical analysis: B.W.K. Obtained funding: J.J.P. Study supervision: J.J.P.

ORCID

Byung-Wook Kim https://orcid.org/0000-0002-2290-4954
Jong Jae Park https://orcid.org/0000-0002-4642-5405
Hee Seok Moon https://orcid.org/0000-0002-8806-2163
Wan Sik Lee https://orcid.org/0000-0002-8021-6228
Ki-Nam Shim https://orcid.org/0000-0003-4004-6292
Gwang Ho Baik https://orcid.org/0000-0003-1419-7484
Yun Jeong Lim https://orcid.org/0000-0002-3279-332X
Hang Lak Lee https://orcid.org/0000-0002-2825-3216
Young Hoon Youn https://orcid.org/0000-0002-0071-229X
Jun Chul Park https://orcid.org/0000-0001-8018-0010
In-Kyung Sung https://orcid.org/0000-0002-3848-5571
Hyunsoo Chung https://orcid.org/0000-0001-5159-357X
Jeong Seop Moon https://orcid.org/0000-0002-5909-8159
Gwang Ha Kim https://orcid.org/0000-0001-9721-5734
Su Jin Hong https://orcid.org/0000-0003-2012-0360
Hyuk Soon Choi https://orcid.org/0000-0002-4343-6950

REFERENCES

1. Uedo N, Takeuchi Y, Yamada T, et al. Effect of a proton pump inhibitor or an H2-receptor antagonist on prevention of bleeding from ulcer after endoscopic submucosal dissection of early gastric cancer: a prospective randomized controlled trial. Am J Gastroenterol 2007;102:1610-1616.
2. Ye BD, Cheon JH, Choi KD, et al. Omeprazole may be superior to famotidine in the management of iatrogenic ulcer after endoscopic mucosal resection: a prospective randomized controlled trial. Aliment Pharmacol Ther 2006;24:837-843.
3. An JY, Kim BW, Kim JS, Park JM, Kim TH, Lee J. The use of endoscopic clipping in preventing delayed complications after endoscopic resection for superficial non-ampullary duodenal tumors. Clin Endosc 2021;54:563-569.
4. Chey WD, Mody RR, Wu EQ, et al. Treatment patterns and symptom control in patients with GERD: US community-based survey. Curr Med Res Opin 2009;25:1869-1878.
5. Jung YS, Kim EH, Park CH. Systematic review with meta-analysis: the efficacy of vonoprazan-based triple therapy on Helicobacter pylori eradication. Aliment Pharmacol Ther 2017;46:106-114.
6. Miwa H, Uedo N, Watari J, et al. Randomised clinical trial: efficacy and safety of vonoprazan vs. lansoprazole in patients with gastric or duodenal ulcers: results from two phase 3, non-inferiority randomised controlled trials. Aliment Pharmacol Ther 2017;45:240-252.
7. Oshima T, Arai E, Taki M, et al. Randomised clinical trial: vonoprazan versus lansoprazole for the initial relief of heartburn in patients with erosive oesophagitis. Aliment Pharmacol Ther 2019;49:140-146.
8. Hamada K, Uedo N, Tonai Y, et al. Efficacy of vonoprazan in prevention of bleeding from endoscopic submucosal dissection-induced gastric ulcers: a prospective randomized phase II study. J Gastroenterol 2019;54:122-130.
9. Tsuchiya I, Kato Y, Tanida E, et al. Effect of vonoprazan on the treatment of artificial gastric ulcers after endoscopic submucosal dissection: prospective randomized controlled trial. Dig Endosc 2017;29:576-583.
10. Takahashi N, Take Y. Tegoprazan, a novel potassium-competitive acid blocker to control gastric acid secretion and motility. J Pharmacol Exp Ther 2018;364:275-286.
11. Cho YK, Choi MG, Choi SC, 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.
12. Choi YJ, Lee YC, Kim JM, 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.

13. 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.
14. Kim SH, Cho KB, Chun HJ, et al. Randomised clinical trial: comparison of tegoprazan and placebo in non-erosive reflux disease. Aliment Pharmacol Ther 2021;54:402-411.
15. Takahashi K, Sato Y, Kohisa J, et al. Vonoprazan 20 mg vs lansoprazole 30 mg for endoscopic submucosal dissection-induced gastric ulcers. World J Gastrointest Endosc 2016;8:716-722.
16. Maruoka D, Arai M, Kasamatsu S, et al. Vonoprazan is superior to proton pump inhibitors in healing artificial ulcers of the stomach post-endoscopic submucosal dissection: a propensity score-matching analysis. Dig Endosc 2017;29:57-64.
17. Kang H, Kim BJ, Choi G, Kim JG. Vonoprazan versus proton pump inhibitors for the management of gastric endoscopic submucosal dissection-induced artificial ulcer: a systematic review with meta-analysis. Medicine (Baltimore) 2019;98:e15860.
18. Miao T, Zhang Y, Bai L, Yang X, Wen X. Vonoprazan vs. lansoprazole for the treatment of endoscopic submucosal dissection induced gastric ulcer: a systematic review and meta-analysis. Rev Esp Enferm Dig 2023;115:168-174.
19. Kawai D, Takenaka R, Ishiguro M, et al. Vonoprazan versus lansoprazole in the treatment of artificial gastric ulcers after endoscopic submucossal dissection: a randomized, open-label trial. BMC Gastroenterol 2021;21:236.
20. Ishii Y, Yamada H, Sato T, et al. Effects of vonoprazan compared with esomeprazole on the healing of artificial postendoscopic submucosal dissection ulcers: a prospective, multicenter, two-arm, randomized controlled trial. Gastroenterol Res Pract 2018;2018:1615092.
21. Sakita T, Fukutomi H. Endoscopic diagnosis. In: Yoshitoshi Y, ed. All about gastric and duodenal ulcer. Tokyo: Nankodo, 1972:200-211.
22. Choi IJ, Lee NR, Kim SG, et al. Short-term outcomes of endoscopic submucosal dissection in patients with early gastric cancer: a prospective multicenter cohort study. Gut Liver 2016;10:739-748.
23. Jenkins H, Sakurai Y, Nishimura A, et al. Randomised clinical trial: safety, tolerability, pharmacokinetics and pharmacodynamics of repeated doses of TAK-438 (vonoprazan), a novel potassium-competitive acid blocker, in healthy male subjects. Aliment Pharmacol Ther 2015;41:636-648.
24. He J, Cao G, Yu J, et al. Safety, tolerability and pharmacokinetics of single ascending and multiple oral doses of tegoprazan in healthy Chinese subjects. Clin Drug Investig 2021;41:89-97.