INTRODUCTION

*Helicobacter pylori* is a flagellated, microaerophilic, gram-negative, spiral-shaped bacterium that colonizes the stomach. It is one of the most common human pathogens and is a significant risk factor for various gastrointestinal diseases, including gastritis, peptic ulcers, gastric cancer, and gastric mucosa-associated lymphoid tissue lymphoma, as well as extragastric diseases, such as idiopathic thrombocytopenic purpura and iron deficiency anemia. Eradicating *H. pylori* infections could, therefore, potentially contribute to public health by reducing the incidence of these diseases.

Adequate acid suppression plays a crucial role in the treatment of *H. pylori* infections because the bacteria transition into a coccoid form at acidic pHs, rendering them resistant to antibiotics. Moreover, maintaining a neutral intragastric pH enhances antibiotic concentrations in the gastric fluid by ensuring drug stability and reducing the minimum inhibitory concentration of antibiotics.
concentrations (MICs). A 14-day triple therapy (TT) consisting of a proton pump inhibitor (PPI), clarithromycin, and amoxicillin is one of the most widely prescribed first-line treatment regimens, worldwide, including in Korea.

Tegoprazan is a novel potassium-competitive acid blocker (P-CAB) that inhibits H⁺/K⁺-ATPase pumps in gastric parietal cells, similar to the action of PPIs. However, unlike PPIs, P-CABs do not require activation by gastric acid, can act on inactive H⁺/K⁺-ATPases, and remain stable at acidic pHs. Furthermore, P-CABs are less influenced by cytochrome P450 2C19 (CYP2C19). Thus, P-CABs are theoretically expected to be more rapid and effective acid blockers than PPIs. The current Japanese guidelines recommend P-CAB-based TT as a first-line regimen.

In March 2020, tegoprazan was approved for the treatment of H. pylori infections in Korea. Unfortunately, limited data are available regarding tegoprazan-based therapy regimens, particularly in real-world settings. We assessed the comparative efficacies tegoprazan- and lansoprazole-based TTs as well as patient adherence to the therapeutic regimens.

**METHODS**

**Patients**

Between March 2020 and February 2023, 670 patients were diagnosed with H. pylori infections and prescribed TT regimens for the treatment of H. pylori at Ilsan Paik Hospital (Goyang, Korea). Patients were excluded from the study if they had previous histories of H. pylori eradication (59 patients), received 7- or 10-day TT regimens (176 patients), or were prescribed acid suppressants other than tegoprazan or lansoprazole (76 patients). Finally, 359 patients who received either 14-day tegoprazan- (tegoprazan group, 64 patients) or lansoprazole-based TT (lansoprazole group, 295 patients) as the first-line treatment for H. pylori infections were included in the study (Fig. 1). The patients’ baseline characteristics; main indications for H. pylori eradication; and treatment outcomes, including the results of H. pylori eradication therapy, treatment regimen adherence, and adverse events (AEs), were retrospectively investigated.

**Diagnosis of H. pylori infection and confirmation of H. pylori eradication**

H. pylori infections were diagnosed using one of the following tests (Supplementary Table 1 in the online-only Data Supplement): rapid urease test (Pyloplus®; ARJ Medical, Oldsmar, FL, USA), histological examination involving modified Giemsa staining, or ¹³C-urea breath test (Otsuka Pharmaceutical, Tokyo, Japan).

Multiple national guidelines recommend the ¹³C-urea breath test for confirming H. pylori eradication. Thus, patients underwent this confirmatory test at least 4 weeks after completion of the medication regimen. Breath samples were collected after the patient had fasted for at least 4 h. A tablet containing 100 mg of ¹³C-urea (UBIT®; Otsuka Pharmaceutical) was administered, per os, with 100 mL of water. Follow-up breath samples were collected 20 min after the tablet had been swallowed. The presence of H. pylori was determined using the collected breath samples (Analyzer POCone; Otsuka Electronics, Japan).
Osaka, Japan). The cutoff value was 2.5%.

**H. pylori eradication therapy**

Current Korean guidelines recommend the empirical treatment of *H. pylori* infections with TT regimens consisting of acid suppression and two antibiotics. The tegoprazan group received tegoprazan (50 mg), amoxicillin (1000 mg), and clarithromycin (500 mg) twice daily for 14 days. The lansoprazole group received lansoprazole (30 mg), amoxicillin (1000 mg), and clarithromycin (500 mg) twice daily for 14 days. Treatment adherence was defined as the administration of at least 80% of the prescribed medications. AEs were classified into three categories: mild (symptoms subsided spontaneously), moderate (symptoms requiring management), and severe (symptoms necessitating emergency room visits).

**Statistical analysis**

All statistical analyses were conducted using R (Version 4.1.1; The R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were analyzed using chi-square or Fisher’s exact tests, as indicated; continuous variables were analyzed using Student’s t-test or the Mann–Whitney U test. *p*-values <0.05 were considered statistically significant. A non-inferiority test was conducted in both the intent-to-treat (ITT) and per-protocol (PP) populations; non-inferiority was declared if the lower limit of the one-sided 95% confidence interval for the difference in eradication rates was above the non-inferiority margin value of -0.1.

**Ethics statement**

Ethics approval for this study was obtained from the Ilsan Paik Hospital Institutional Review Board (approval number 2022-10-007-001). The requirement for informed consent was waived due to the retrospective nature of the study.

**RESULTS**

**Baseline characteristics**

Table 1 presents the baseline characteristics of the 359 patients in the tegoprazan (64 patients) and lansoprazole (295 patients) groups. There were no significant differences in ages or sex distributions between the two groups. The most common indication for treatment in both groups was *H. pylori*-associated gastritis, followed by peptic ulcers.

**Adherence and AEs**

In the tegoprazan group, nine patients were lost to follow-up and one received insufficient medication (<80% of the prescribed medications). In the lansoprazole group, 42 patients were lost to follow-up, and two received insufficient medication (Fig. 1). Consequently, the adherence rates of the patients in the tegoprazan and lansoprazole groups were 84.4% (54/64) and 85.1% (251/295), respectively (Fig. 2); no significant difference was observed (*p*=0.78).

The AEs associated with tegoprazan-based TT are shown in Table 2. The overall AE rate was 23.4% (15/64). The most common AE was diarrhea (7.8%), followed by dysgeusia (6.3%). Of 100

![Fig. 2. The adherence rates for tegoprazan- and lansoprazole-based triple therapies.](image-url)
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The overall H. pylori eradication rates were 75.8% (272/359) in the ITT population and 88.5% (270/305) in the PP population. In the ITT population, the H. pylori eradication rates for patients in the tegoprazan- and lansoprazole groups were 76.6% (49/64) and 75.6% (223/295), respectively (Fig. 3). The lower limit of the one-sided 95% confidence interval for the difference in eradication rates was -0.087, which was above the non-inferiority margin of -10% ($p=0.03$). In the PP population, the eradication rates for patients in the tegoprazan- and lansoprazole groups were 88.9% (48/54) and 88.4% (222/251), respectively (Fig. 3); the lower limit of the one-sided 95% confidence interval (-0.074) was also above the non-inferiority margin of -10% ($p=0.01$).

DISCUSSION

P-CABs are known for their more rapid and potent acid-suppressing properties compared with PPIs. P-CABs have demonstrated superior or comparable efficacies in the treatment of various acid-related diseases, such as gastroesophageal reflux disease and peptic ulcers, for which PPIs are commonly used. In the context of H. pylori treatment, the stronger antisecretory potency of P-CABs is expected to increase antibiotic stability in the gastric fluid and reduce antibiotic MICs, thereby elevating the eradication rate.

Vonoprazan is a P-CAB approved and prescribed for first-line treatment of H. pylori infections in Japan. Recently, a number of studies have been published regarding vonoprazan-based H. pylori eradication therapy. Even in cases involving clarithromycin-resistant H. pylori strains, vonoprazan-based TT showed an eradication rate of 82.0%, whereas the eradication rate of the comparator lansoprazole-based TT was 40.0%. The strong acid suppression provided by vonoprazan appears to help TT regimens overcome the challenge of clarithromycin-resistant H. pylori strains. Furthermore, recent meta-analyses have indicated the superiority of vonoprazan-based therapy over PPI-based therapy.

In our study, the 14-day tegoprazan-based TT demonstrated H. pylori eradication rates of 76.6% and 88.9% in the ITT and PP populations, respectively. The eradication rates for the 14-day lansoprazole-based TT were 75.6% and 88.4% in the ITT and PP populations, respectively. In contrast to the reported superiority of vonoprazan for H. pylori eradication, our study failed to demonstrate the superiority of tegoprazan over lansoprazole; rather, the tegoprazan-based TT was deemed non-inferior to the lansoprazole-based TT. There are several possible reasons for this finding. First, the clarithromycin MIC distribution for H. pylori may vary according to geographic region. Such differences in antibiotic resistance between the Korean and Japanese population could contribute to different efficacies. Second, the pharmacological differences between tegoprazan and vonoprazan, such as half-lives or maximum plasma concentrations, may limit the efficacy of tegoprazan. Moreover, twice daily 50-mg tegoprazan doses may be insufficient to achieve the necessary acid suppression and overcome clarithromycin resistance. A previous randomized clinical trial demonstrated that tegoprazan increases intragastric pH in a dose-dependent manner; the mean values of the 15-minute median intragastric pH over 24 h on day 7 was 5.2 with a 100-mg daily dose of tegoprazan and 6.4 with a 200-mg daily dose. Therefore, increasing the tegoprazan dose to 100 mg twice daily may improve H. pylori eradication rates.

Poor therapeutic compliance is one reason for eradication failure. In our study, 1.6% and 0.7% of the patients in the tegoprazan and lansoprazole groups, respectively, received insuf-

Table 2. Adverse events of 14-day tegoprazan-based triple therapy

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Value (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse events</td>
<td>15 (23.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (7.8)</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>4 (6.3)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Constipation</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (1.6)</td>
</tr>
</tbody>
</table>

Data are presented as n (%).
efficient medication (<80% of the prescribed medications). Additionally, 14.1% and 14.2% of patients in the tegoprazan and lansoprazole groups, respectively, were lost to follow-up. Consequently, the adherence rates were similar for the tegoprazan (84.4%) and lansoprazole (85.1%) groups (p=0.78). Unfortunately, we were unable to investigate the AEs or other factors potentially contributing to patients being lost to follow-up due to the absence of relevant medical records.

AEs are among the most common factors leading to poor compliance. Hepatotoxicity concerns were associated with the earlier P-CABs, leading to their discontinued clinical development. However, vonoprazan showed similar rates of liver function abnormalities compared with lansoprazole during an 8-week treatment for erosive esophagitis, with no reported increase in hepatotoxicity during 52 weeks of maintenance therapy. Furthermore, the safety profile of vonoprazan during long-term use was similar to that of lansoprazole. Similarly, tegoprazan exhibited no significant difference in liver toxicity rates compared with lansoprazole, and its safety profile was similar to that of lansoprazole over a 24-week period. Multiple randomized controlled trials have reported gastrointestinal disorders, including diarrhea and nausea, as the most common AEs associated with tegoprazan use, with the majority having mild intensity. Likewise, previous studies investigating tegoprazan-based TT regimens have shown most AEs to be mild, requiring no medical management, with the most frequent ones being gastrointestinal disorders. Our study found a 23.4% rate of AEs associated with tegoprazan-based TT, consistent with prior studies. Owing to the lack of relevant medical records, AE rates for lansoprazole-based TT could not be determined.

To date, four studies have compared tegoprazan and PPIs for the treatment of H. pylori infections. Kim et al. compared the efficacy of a 7-day tegoprazan-based TT regimen (tegoprazan [50 mg], clarithromycin [500 mg], amoxicillin [1000 mg]) combined with twice daily bismuth (bismuth potassium citrate [300 mg]) against a lansoprazole-based TT regimen that replaced tegoprazan with lansoprazole (30 mg). In both the ITT and PP analyses, the H. pylori eradication rates were not significantly different, consistent with our findings (78.8% vs. 74.5% with p=0.323 in the ITT analysis and 88.3% vs. 82.8% with p=0.151 in the PP analysis). However, the regimen employed by Kim et al. (standard TT regimen plus bismuth) is not commonly prescribed in clinical practice and is not a recommended first-line treatment. Choi et al. conducted a randomized controlled trial comparing 7-day tegoprazan- and lansoprazole-based TTs. They demonstrating that tegoprazan is as effective as lansoprazole for eradicating H. pylori treatment, with eradication rates of 62.86% and 60.57%, respectively, in the ITT populations and 69.33% and 67.33%, respectively, in the PP populations. Their observed eradication rates were lower than those observed in our study. We believe that the extended 14-day treatment duration in our study contributed to the observed higher eradication rates. To improve eradication rates, the current Korean guidelines recommends 14-day TT regimens as first-line treatments. In a retrospective study, Jung et al. reported similar efficacies for 14-day tegoprazan- and rabeprazole-based TTs. The eradication rates of the tegoprazan- and rabeprazole-based regimens were 76.7% and 75.4%, respectively, in the ITT population and 83.4% and 83.5%, respectively, in the PP population, similar to our findings. Kim et al. showed the non-inferiority of tegoprazan-based bismuth quadruple therapy to lansoprazole-based quadruple therapy as first-line H. pylori eradication treatments in a randomized controlled trial (80.0% vs. 77.4%, respectively, in the ITT analysis; 90.2% vs. 82.4%, respectively, in the PP analysis). In addition, a recent retrospective study comparing tegoprazan with the combination of a PPI and an antacid for H. pylori eradication was published in 2023. It showed no significant difference in the eradication rates between 14-day tegoprazan- and esomeprazole/sodium bicarbonate-based TTs (ITT population: 78.6% vs. 81.4%, respectively, p=0.313; PP population: 85.5% vs. 87.8%, respectively, p=0.339). Our study provides additional support for the non-inferior efficacy of the tegoprazan-based regimen as a first-line treatment for H. pylori eradication.

Our study had several limitations. First, this was a single-center retrospective observational study, which limits the generalizability of our findings. Second, the tegoprazan group had a relatively small sample size, which may have lowered the statistical power for assessing treatment efficacy. Third, adverse reactions and reasons for non-adherence were not examined due to the lack of medical records. Instead, we evaluated medication adherence and found no significant difference between tegoprazan and lansoprazole. Finally, antibiotic susceptibility tests were not performed, preventing an assessment of the efficacy of tegoprazan-based TT against clarithromycin-resistant H. pylori strains. However, we believe that the lack of antibiotic susceptibility data does not limit the clinical significance of our study as empirical therapy is commonly employed in real-world settings and continues to be recommended by guidelines.

In conclusion, 14-day tegoprazan-based TT was non-inferior to 14-day lansoprazole-based TT as a first-line treatment for H. pylori eradication. Thus, tegoprazan may serve as an alternative to PPIs for eradicating H. pylori.

Supplementary Materials
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