



Evaluation of the Efficacy and Safety of a Dual Delayed-Release Formulation of 10-mg Esomeprazole in Patients with Gastric Erosions: A Multicenter, Randomized, Double-Blind, Active-Control, Phase III Study

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Background/Aims: Clinical data on the efficacy and safety of the dual delayed-release formulation of 10-mg esomeprazole (HIP2101) are currently limited. Therefore, this study compared the efficacy and safety of HIP2101 and 20-mg famotidine (RLD2101) in patients with gastric erosions.

Methods: In this multicenter, randomized, double-blind, active-control, phase III study, 326 patients with endoscopically proven gastric mucosal erosion were randomly assigned to receive either HIP2101 or RLD2101 once daily for 2 weeks. The primary endpoint was the rate of improvement of erosion. Secondary endpoints (rate of cure of erosion and edema, and rate of improvement of hematin and gastrointestinal symptoms) and treatment-emergent adverse events were compared between the groups.

Results: Based on the per-protocol set (PPS) analysis, the improvement rates for erosion were 64.9% (98/151) and 63.7% (100/157) in the HIP2101 and RLD2101 groups, respectively (95% confidence interval, -9.5 to 11.9). The lower bound of the 95% confidence interval was greater than the noninferiority margin of -14%. These results were similar to those of the full analysis set (FAS) (HIP2101 group, 64.6%; RLD2101 group, 62.7%). Based on the PPS and FAS analyses, the cure rates for erosion and edema and the improvement rates for hematin and gastrointestinal symptoms were comparable between the groups. The number of adverse events did not differ significantly between the groups.

Conclusions: The efficacy and safety of HIP2101 were comparable to those of RLD2101 in the treatment of gastric erosions and symptomatic improvement. These findings suggest that HIP2101 may be a novel treatment option for gastritis (ClinicalTrials.gov identifier: NCT05024721). (*Gut Liver*, 2025;19:519-527)

Key Words: Proton pump inhibitors; HIP2101; Esomeprazole; Gastritis; RLD2101



INTRODUCTION

Gastritis, defined histologically by infiltration of inflammatory cells in the gastric mucosa, is a commonly diagnosed condition in clinical practice.^{1,2} While various causes lead to gastritis, acute gastritis can be attributed to external causes, such as medication, alcohol consumption, and stress, as well as internal causes, including allergies and bacterial infections.³ In contrast, chronic gastritis is increasingly associated with *Helicobacter pylori* infection as the most substantial cause.³ Although most cases of gastritis resolve without complications, it can lead to serious issues if left untreated or exacerbated by certain factors, such as peptic ulcer disease, gastrointestinal bleeding, anemia, and in rare cases of gastric cancer.³

The treatment of gastritis typically involves addressing the underlying causes; however, identifying the exact causes can be difficult. Therefore, gastric acid is considered to be the primary cause of gastritis. According to most clinical guidelines, treating gastritis commonly involves the use of medications such as histamine-2 receptor antagonists (H₂RAs) and proton pump inhibitors (PPIs) to reduce gastric acid secretion, along with antacids to neutralize the acid.^{4,5} Compared with other medications, PPIs have more potent effects on acid-related diseases. However, data on the efficacy of low-dose PPI in the treatment of gastritis are limited. Dual delayed-release formulation of 10-mg esomeprazole (HIP2101) is a low-dose formulation of esomeprazole with dual delayed-release. Compared to conventional delayed-release PPIs, HIP2101 offers a longer duration of action and a consistent effect regardless of food intake, as demonstrated in previous pharmacokinetic and pharmacodynamic studies conducted in healthy subjects.^{6,7} These characteristics suggest potential improvements in the efficacy of treatments for acid-related diseases, including gastritis. However, clinical data on the efficacy and safety of HIP2101 are currently limited.

Therefore, this clinical trial aimed to evaluate the efficacy and safety of HIP2101 in treating patients with gastric erosions by assessing whether there is non-inferiority of HIP2101 compared to 20-mg famotidine (RLD2101) in terms of the efficacy of reducing mucosal erosion, as observed in endoscopic examinations after the 2-week treatment.

MATERIALS AND METHODS

1. Ethics statements

This study was carried out in accordance with the recommendations of the Declaration of Helsinki. The study

protocol was approved by the ethics committees of all participating hospitals including Asan Medical Center (IRB number: 2021-0745), and written informed consent was obtained from each patient before enrollment. This trial was registered with ClinicalTrials.gov (registration number: NCT05024721).

2. Study design and population

This multicenter, randomized, double-blind, active-control, phase III study involved patients diagnosed with gastric erosions at 22 hospitals in the Republic of Korea between August 2021 and March 2022. Patients who met the following criteria were enrolled: (1) aged 19 to 75 years at the time of consent; (2) diagnosed with acute or chronic gastritis on the basis of endoscopy showing one or more observed erosions; and (3) voluntarily signed an informed consent form.

The exclusion criteria were as follow: (1) patients with active gastric or duodenal ulcer, reflux esophagitis, Barrett esophagus (>3 cm), or esophagogastric varices at the time of screening endoscopy; (2) patients who underwent surgical intervention for the gastric or esophageal diseases; (3) patients who experienced the following conditions within the past 3 months: Zollinger–Ellison syndrome, esophageal obstruction, esophageal motility disorders, inflammatory bowel disease, acute pancreatitis, liver dysfunction (aspartate aminotransferase or alanine transaminase >3 times the upper limit of normal), renal dysfunction (Modification of Diet in Renal Disease estimated glomerular filtration rate <30 mL/min/1.73 m²), history of thrombosis (including cerebral thrombosis, myocardial infarction, and venous thrombosis), or blood clotting disorders; (4) patients who received the following medications within 2 weeks before screening endoscopy or required continuous administration of them during the clinical trial period: acid-suppressive agents (H₂RAs, PPIs, potassium-competitive acid blockers, and antacids), mucosal protective agents, and anticholinergics; (5) patients who received the following medications within 1 week before screening endoscopy or required continuous administration of anti-thrombotics; and (6) patients who required continuous administration of them during the clinical trial period: non-steroidal anti-inflammatory drugs, corticosteroids, bisphosphonates, and iron supplements. Additional exclusion criteria can be found at ClinicalTrials.gov (registration number: NCT05024721).

Patients diagnosed with acute or chronic gastritis on the basis of endoscopy revealing one or more observed erosions were randomly assigned to receive either HIP2101 or RLD2101 once daily for 2 weeks. After 2 weeks of treatment, the non-inferiority of HIP2101 to RLD2101 was

evaluated, as assessed by the erosion score on endoscopy. *H. pylori* infection was evaluated using either the rapid urease test, histological examination, or the ^{13}C -urea breath test.

3. Efficacy and safety assessment

Patients who met all the selection criteria were stratified by institution and randomly assigned at a 1:1 ratio to either the HIP2101 or RLD2101 group. The patients received the investigational product (IP) (HIP2101 in the morning or RLD2101 before bedtime) for 2 weeks. To maintain blinding of the investigators and patients, the appearance of each placebo was identical to that of HIP2101 (capsule) and RLD2101 (tablet). After completing the 2-week treatment period, the participants visited the investigational site for efficacy and safety evaluations, including endoscopy and assessment of gastrointestinal symptoms.

The primary endpoint of this study was the improvement rate of erosion at week 2. After the 2-week treatment, an improvement in the erosion score (1, no visible erosion; 2, one or two erosions; 3, three to five erosions; 4, more than six erosions) by $>50\%$ compared with that before administration was considered effective. The improvement rate of erosion was calculated as follows: improvement rate of erosion (%) = (number of improved patients/number of analyzed patients) $\times 100$.

Secondary endpoints included the cure rate of erosion and edema, improvement rate of hematin and improvement rate of gastrointestinal symptoms between the HIP2101 and RLD2101 treatment groups at 2 weeks. The cure rate of erosion or edema (1, none; 2, pale/whiter and slightly accentuated hexagonal area gastric pattern) was defined as the percentage of patients whose erosion or edema was completely cured on endoscopic examination after the 2-week treatment (Fig. 1). The improvement rate of hematin or gastrointestinal symptoms was defined by the percentage of patients whose hematin (1, none; 2, single hematin; 3, two to five hematin; 4, six to 10 hematin; 5, >10 hematin or large area of a confluent hematin) or gastrointestinal symptom (frequency: 0, absent; 1, one or two times a week; 2, three or four times a week; 3, five or six times a week; 4, daily) (severity: 0, none; 1, mild; 2, moderate; 3, severe; 4, very severe) score improved by $>50\%$ (Fig. 1).

4. Statistical analysis

Currently, no clinical data are available on the improvement rate of conventional PPIs for gastric erosion. Therefore, H_2RA was selected as the control group in this study.⁸ The improvement rate of HIP2101 is expected to be non-inferior to that of RLD2101. Based on these assumptions, the sample size for the trial was calculated assuming an im-

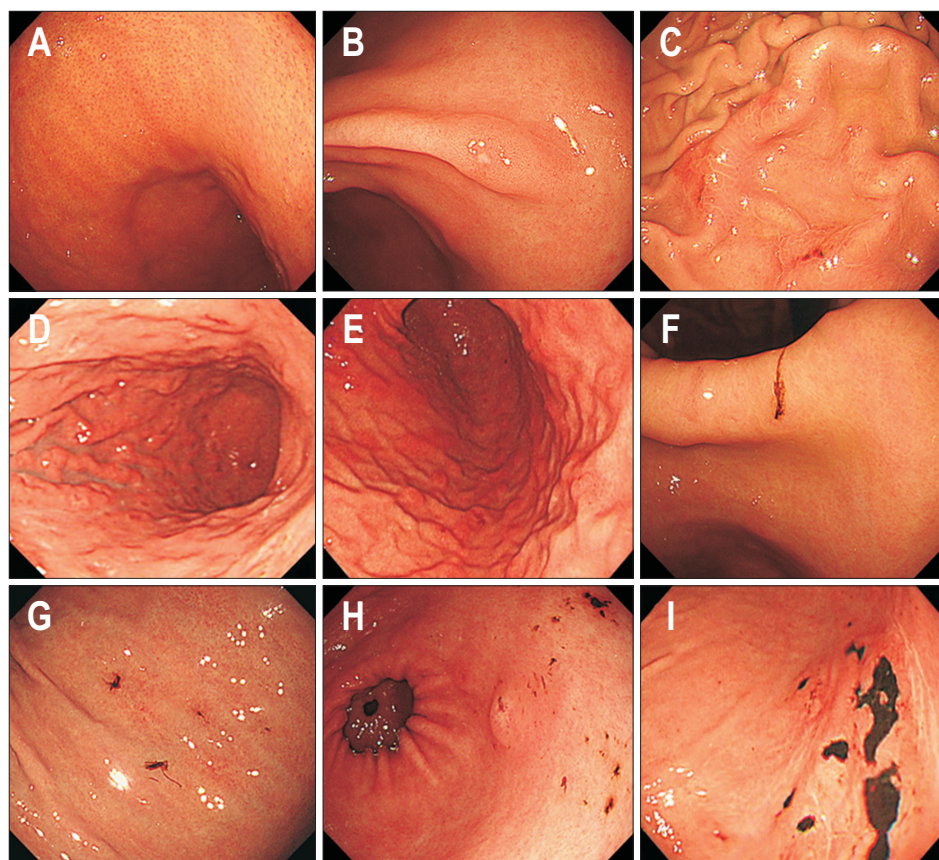


Fig. 1. Representative endoscopic images for each grade of erosion [A: score 1, B: score 2, C: score 3, D: score 4], edema [E: score 2], and hematin [F: score 2, G: score 3, H: score 4, I: score 5].

provement rate of erosion of 79.1% for the investigational drug and comparator, a non-inferiority margin of 14%, a significance level of 0.025, and power of 80%. The results of the sample size calculation indicated that 133 participants were required per treatment group. Considering a dropout rate of 18%, 163 participants were recruited per treatment group, totaling 326 participants.

The primary efficacy evaluation of this clinical trial was conducted according to the clinical trial protocol, with the per-protocol set (PPS) of patients who completed the clinical trial designated as the main analysis group. Patients with major protocol violations or poor compliance (taking <70% of the total medications) were excluded from the PPS. Compliance was assessed by counting the number of unused medications after 2 weeks of treatment. The full analysis set (FAS), which included all patients who received at least one dose of the investigational drug and underwent primary efficacy assessments at least once until the end of the clinical trial, was the supplementary analysis group. Secondary efficacy evaluation involved analyzing both analysis groups and presenting the results. A safety evaluation was conducted on the safety analysis set, comprising

participants who received at least one dose of the clinical trial drugs after random assignment and for whom safety assessment data could be obtained.

The chi-square test or Fisher exact test was used to test for associations among various categorical variables, whereas the independent sample t-test or Wilcoxon rank-sum test was used for non-categorical variables. Statistical analyses were performed using SAS (version 9.4, SAS Institute, Cary, NC, USA), and a p-value <0.05 was considered statistically significant.

RESULTS

1. Baseline characteristics

A total of 326 patients were enrolled in this clinical trial (Fig. 2). All patients were included in the safety analysis. Among them, 319 patients (158 and 161 in the HIP2101 and RLD2101 groups, respectively) were included in the FAS, and 308 patients (151 and 157 in the HIP2101 and RLD2101 groups, respectively) were included in the PPS (7 took the IP <70% of the time, 1 took the IP for >14 days, 2

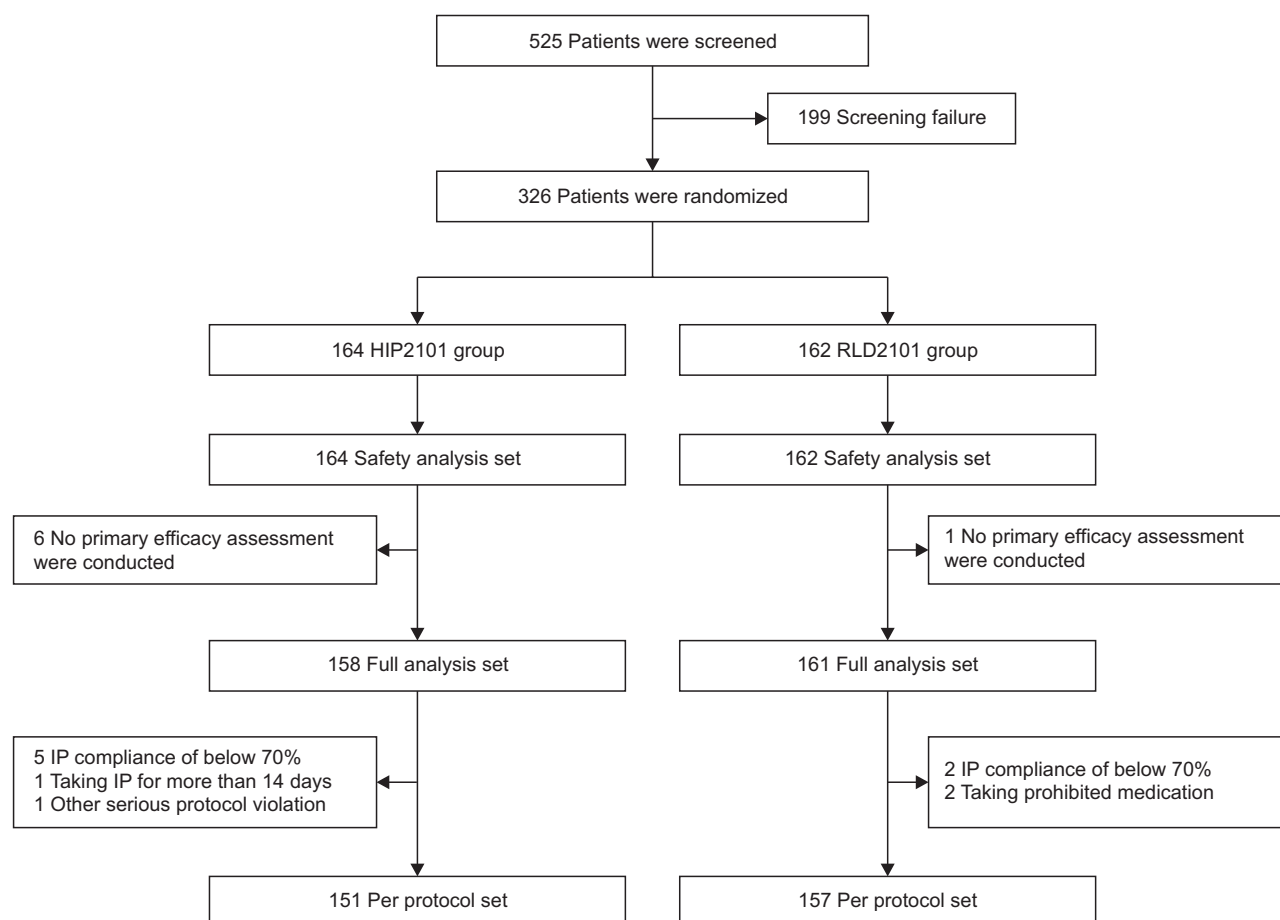


Fig. 2. Randomization protocol and patient disposition. HIP2101, 10-mg esomeprazole; RLD2101, 20-mg famotidine; IP, investigational product.

Table 1. Baseline Patient Characteristics

Characteristic	Treatment*		Total (n=319)	p-value
	HIP2101 (n=158)	RLD2101 (n=161)		
Age, yr	43.7±13.0	41.1±11.9	42.4±12.5	0.077 [†]
Male sex	55 [34.8]	59 [36.6]	114 [35.7]	0.732 [‡]
Height, cm	165.2±8.4	165.4±8.4	165.3±8.4	0.754 [†]
Weight, kg	65.2±14.3	66.2±13.1	65.7±13.7	0.382 [†]
Current smoker	20 [12.7]	18 [11.2]	38 [11.9]	0.684 [‡]
Current drinker	88 [55.7]	90 [55.9]	178 [55.8]	0.971 [‡]
Classification of gastritis				0.961 [‡]
Acute	82 [51.9]	84 [52.2]	166 [52.0]	
Chronic	76 [48.1]	77 [47.8]	153 [48.0]	
<i>Helicobacter pylori</i> infection	37 [23.4]	35 [21.7]	72 [22.6]	0.720 [‡]
Total number of erosions	3.4±2.7	3.2±2.5	3.3±2.6	0.687 [†]
Grade of erosion				0.991 [‡]
Score 2	78 [49.4]	80 [49.7]	158 [49.5]	
Score 3	57 [36.1]	57 [35.4]	114 [35.7]	
Score 4	23 [14.6]	24 [14.9]	47 [14.7]	
Grade of edema				0.790 [‡]
Score 1	114 [72.2]	114 [70.8]	228 [71.5]	
Score 2	44 [27.8]	47 [29.2]	91 [28.5]	
Grade of hematin				0.448 [§]
Score 1	128 [81.0]	121 [75.2]	249 [78.1]	
Score 2	11 [7.0]	14 [8.7]	25 [7.8]	
Score 3	14 [8.9]	23 [14.3]	37 [11.6]	
Score 4	3 [1.9]	1 [0.6]	4 [1.3]	
Score 5	2 [1.3]	2 [1.2]	4 [1.3]	
Gastrointestinal symptoms scores				
Frequency	4.4±3.7	4.1±3.1	4.2±3.4	0.988 [†]
Severity	4.1±3.4	4.0±2.9	4.1±3.1	0.834 [†]
Treatment compliance, %				
Morning	95.8±7.7	96.5±6.6	96.1±7.1	0.589 [†]
Night	93.3±8.7	94.8±8.0	94.1±8.4	0.148 [†]

Data are presented as the mean±SD or the number (%). Analysis population is the full analysis set.

*Treatments: HIP2101=esomeprazole 10 mg and RLD2101=famotidine 20 mg; [†]Wilcoxon rank-sum test; [‡]Pearson chi-square test; [§]Fisher exact test.

took prohibited medication, and 1 violated the protocol).

Table 1 summarizes the baseline patient demographics and other characteristics according to the treatment group. Of the 319 patients, 166 (52.0%) and 153 (48.0%) had acute and chronic gastritis, respectively. The mean number of erosions was 3.3, and there were no significant differences in baseline characteristics or endoscopic findings of gastritis between the groups. The overall compliance rates with the morning and night IP were 96.1% and 94.1%, respectively, with no statistically significant difference between the groups ($p=0.589$ and $p=0.148$, respectively).

2. Primary endpoint assessment

On the basis of the PPS analysis, the improvement rate of erosion in the HIP2101 group was 64.9% (98/151), which was higher than that of 63.7% (100/157) in the RLD2101 group (Table 2). The 95% confidence interval (CI) of the difference between the groups ranged from −9.5

to 11.9. In the FAS analysis, the improvement rate of erosion (64.6%, 102/158) in the HIP2101 group was higher than that (62.7%, 101/161) in the RLD2101 group, and the 95% CI of the difference ranged from −8.7 to 12.4. The lower bounds of the two-sided 95% CI for the PPS and FAS analyses were −9.5% and −8.7%, respectively, and the lower bounds of the 95% CI were greater than the non-inferiority margin of −14%. Thus, the non-inferiority of HIP2101 compared to RLD2101 was demonstrated.

3. Secondary endpoints assessment

1) Cure rate of erosion and edema

The cure rates of erosion and edema were comparable between the groups in the PPS and FAS analyses (Table 3). In the PPS analysis, the cure rates of erosion in the HIP2101 and RLD2101 groups were 55.6% (84/151) and 59.2% (93/157), respectively ($p=0.522$). Similarly, in the FAS analysis, the cure rates of erosion were 55.7% (88/158)

Table 2. Rate of Improvement of Erosion after 2-Week Treatment (Noninferiority)

Analysis	Improvement rate of erosion	Difference (%) from RLD2101	95% CI on the difference*	p-value [†]
Per-protocol set				
HIP2101 (n=151) [‡]	98 (64.9)	1.2	-9.5 to 11.9	0.003
RLD2101 (n=157) [‡]	100 (63.7)			
Full analysis set				
HIP2101 (n=158) [‡]	102 (64.6)	1.8	-8.7 to 12.4	0.002
RLD2101 (n=161) [‡]	101 (62.7)			

Data are presented as the number (%).

*Noninferiority margin of -14%; [†]p-value for the noninferiority test; [‡]Treatments: HIP2101=esomeprazole 10 mg and RLD2101=famotidine 20 mg.

Table 3. Secondary Efficacy Analysis

Analysis	Treatment*		p-value
	HIP2101	RLD2101	
Per-protocol set			
Cure rate of erosion	84/151 (55.6)	93/157 (59.2)	0.522 [§]
Cure rate of edema [†]	35/43 (81.4)	30/46 (65.2)	0.086 [§]
Improvement rate of hematin [†]	25/30 (83.3)	36/39 (92.3)	0.281
Improvement rate of GI symptoms [†]			
Frequency	98/136 (72.1)	94/140 (67.1)	0.375 [§]
Severity	99/136 (72.8)	96/140 (68.6)	0.441 [§]
Full analysis set			
Cure rate of erosion	88/158 (55.7)	93/161 (57.8)	0.709 [§]
Cure rate of edema [†]	35/44 (79.5)	31/47 (66.0)	0.147 [§]
Improvement rate of hematin [†]	25/30 (83.3)	37/40 (92.5)	0.275
Improvement rate of GI symptoms [†]			
Frequency	103/143 (72.0)	95/144 (66.0)	0.267 [§]
Severity	104/143 (72.7)	98/144 (68.1)	0.386 [§]

Data are presented as the number/number (%).

*Treatments: HIP210=esomeprazole 10 mg and RLD2101=famotidine 20 mg; [†]Number of subjects with a score of ≥ 2 at visit 1; [‡]Number of subjects with a gastrointestinal (GI) symptom total score of ≥ 1 at visit 2; [§]Pearson chi-square test; ^{||}Fisher exact test.

in the HIP2101 group and 57.8% (93/161) in the RLD2101 group ($p=0.709$). In the PPS analysis, the cure rates of edema after 2 weeks of treatment were 81.4% (35/43) in the HIP2101 group and 65.2% (30/46) in the RLD2101 group ($p=0.086$). In the FAS analysis, the cure rates of edema were 79.5% (35/44) in the HIP2101 group and 66.0 (31/47) in the RLD2101 group ($p=0.147$).

2) Improvement rate of hematin and gastrointestinal symptoms

The improvement rate of hematin was also evaluated (Table 3). Although the improvement rate of hematin in the HIP2101 group was lower than that in the RLD2101 group in the PPS (83.3% and 92.3%, respectively, $p=0.281$) and FAS analyses (83.3% and 92.5%, respectively, $p=0.275$), the difference was not statistically significant.

The improvement rate of gastrointestinal symptoms, including frequency and severity, was assessed (Table 3). After 2 weeks of treatment, according to the PPS analysis, the improvement rates of gastrointestinal symptom frequency and severity were 72.1% (98/136) and 72.8% (99/136) in

the HIP2101 group and 67.1% (94/140) and 68.6% (96/140) in the RLD2101 group, respectively ($p=0.375$ and $p=0.441$, respectively). In the FAS analysis, the improvement rates of gastrointestinal symptom frequency and severity were 72.0% (103/143) and 72.7% (104/143) in the HIP2101 group and 66.0% (95/144) and 68.1% (98/144) in the RLD2101 group, respectively ($p=0.267$ and $p=0.386$, respectively).

3. Efficacy and safety assessment

Nine patients in the HIP2101 group (5.5%, 11 events) and 11 patients in the RLD2101 group (6.8%, 21 events) reported treatment-emergent adverse events (Table 4). Among these, six patients in the HIP2101 group (3.7%) and four patients in the RLD2101 group (2.5%) were confirmed to have drug-related adverse events. Most treatment-emergent adverse events were rated as mild or moderate in severity, except for one case of subarachnoid hemorrhage, which was considered unrelated to the study drug (HIP2101) by the investigator (Supplementary Table 1).

Table 4. Treatment-Emergent Adverse Events

Variable	Treatment*		Total (n=326)
	HIP2101 (n=164)	RLD2101 (n=162)	
No. of subjects with TEAEs	9 (5.5)	11 (6.8)	20 (6.1)
Intensity			
Mild	7 (4.3)	10 (6.2)	17 (5.2)
Moderate	1 (0.6)	1 (0.6)	2 (0.6)
Severe	1 (0.6)	0	1 (0.3)
Relationship			
Yes	6 (3.7)	4 (2.5)	10 (3.1)
No	3 (1.8)	7 (4.3)	10 (3.1)
No. of subjects with serious TEAEs	1 (0.6)	0	1 (0.3)

Data are presented as number (%). Analysis population is the safety analysis set.

TEAEs, adverse events that start after administration of study drug, or preexisting conditions that worsened after administration of study drug.

*Treatments: HIP2101=esomeprazole 10 mg and RLD2101=famotidine 20 mg.

DISCUSSION

Gastritis is an inflammation of the stomach lining that leads to epithelial cell damage and various symptoms and complications. Therefore, treatment goals for gastritis are to achieve mucosal healing, relieve abdominal symptoms, and prevent complications. In most clinical guidelines, the treatment of gastritis includes removal of the causative agent and a limited course of acid suppression with PPIs.^{4,5} However, data on the efficacy of PPIs for the management of gastritis are limited. Additionally, there is no consensus on treatment regimens and appropriate dosages of PPIs. Here, we demonstrated the efficacy and safety of HIP2101 for treating gastritis with erosion and improving gastritis symptoms. Our study showed that the efficacy and safety profile of HIP2101 is comparable with that of RLD2101.

PPIs were introduced clinically more than 35 years ago and have since proven to be invaluable, safe, and effective agents for managing various acid-related disorders due to their potent antisecretory effects. Moreover, recent studies suggest that PPIs may possess antioxidant properties and exert direct effects on various cells involved in inflammation, potentially aiding in the prevention or management of gastritis.⁹ On the basis of these mechanisms, PPIs can be the best option to treat or prevent gastritis. However, conventional delayed-release PPIs have several limitations for treating gastritis: slow onset, short half-life, drug-drug interactions, and dependency on food for efficacy.¹⁰ HIP2101 is a newly developed esomeprazole formulation with dual delayed-release. Compared with conventional delayed-release PPIs, HIP2101 has an extended duration of

therapeutic plasma drug concentration and consistent effects regardless of diet.^{6,7} Therefore, HIP2101 is expected to be a more effective choice for the treatment of gastritis.

Gastric erosion, histologically defined as a superficial mucosal defect that does not penetrate the submucosa, can occur during severe exacerbations of acute and chronic gastritis due to an imbalance between aggressive and protective factors in the gastric mucosa. Gastric acid is the primary aggressive factor influencing the development and healing of gastric erosion. Although potassium-competitive acid blockers have recently been developed and have demonstrated superior efficacy in controlling gastric acid secretion compared to H₂RA and PPIs, H₂RAs and PPIs remain the most commonly prescribed antisecretory drugs for acid-related diseases.^{4,5,11,12} H₂RAs have long been used as the primary treatment for gastritis, demonstrating a rapid onset of action and excellent therapeutic outcomes within a short period of 1 or 2 weeks. However, they exhibit tolerance with repeated dosing.¹³ Compared with H₂RAs, PPIs are characterized by an increased efficacy in suppressing gastric acid secretion with repeated dosing.¹³ In the present study, the improvement rates of erosion in the HIP2101 group were 64.9% in the PPS analysis and 64.6% in the FAS analysis. In addition, we demonstrated that HIP2101 was comparable to RLD2101 in the treatment of gastritis with erosion after a short 2-week treatment.

PPIs typically demonstrate dose-dependent acid suppression.¹⁴ The treatment of acid-related diseases requires varying levels of acid suppression depending on the specific condition and severity. Therefore, the prescribed dose of PPIs is often tailored to an individual patient's condition, considering factors such as the severity of symptoms, extent of acid-related damage, and desired level of acid suppression. Most guidelines recommend the use of lower doses of PPI to reduce potential complications. HIP2101 is the lowest clinically available dose of esomeprazole. On the basis of the results of a previous clinical trial in healthy individuals, HIP2101 achieved a gastric pH of >4 for 35.8% of the 24-hour period following administration over 7 days.¹⁵ In our study, HIP2101 effectively suppressed acid in gastritis, as evidenced by its high cure rate for erosion and edema and improvement rate for hematin and gastrointestinal symptoms. PPS and FAS analyses showed comparable outcomes between the HIP2101 and RLD2101 groups.

In addition to efficacy, the safety of HIP2101 remains a critical consideration. Recent reports suggest the potential long-term adverse effects of PPIs, including community-acquired pneumonia, *Clostridium difficile* infection, atrophic gastritis, and gastric cancer due to gastric acid suppression.¹⁶ Complications of PPIs might be associated with their acid-suppressive potential. In our study, although the

safety of HIP2101 could not be directly compared with higher doses of esomeprazole because of the study design, no severe drug-related adverse events occurred during the 2-week treatment period. Most adverse events were mild to moderate, and there were no significant differences compared to RLD2101.

This study has several limitations. First, we did not compare the long-term efficacy between the groups because of the study design. Second, although medical history and laboratory test results can provide valuable insights, histological diagnosis using endoscopic biopsy is the gold standard for the diagnosis of gastritis. We did not observe any improvement in histological inflammation. Third, H₂RA was selected as the control group for this study. However, due to differences in mechanisms of action and efficacy profiles between PPIs and H₂RAs, comparisons between these classes may be considered unconventional. Limited data on the healing effects of conventional PPIs for gastric erosion made them less suitable as a control group and posed challenges for accurate sample size estimation.

In conclusion, this study demonstrated the efficacy and safety of HIP2101 as a treatment option for gastric erosions. The results indicated that HIP2101 was non-inferior to RLD2101 in terms of efficacy, and its safety profile was comparable to that of RLD2101, as evidenced by the improved rate of erosion and tolerability profiles. These findings suggest that HIP2101 is a novel treatment option for gastritis.

CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

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

Y.L., S.H.H. Statistical analysis: H.Y.J., Y.L., S.H.H. Administrative, technical, or material support; study supervision: H.Y.J., Y.L., S.H.H. Approval of final manuscript: all authors.

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SUPPLEMENTARY MATERIALS

Supplementary materials can be accessed at <https://doi.org/10.5009/gnl240390>.

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