Efficacy and Safety of Vonoprazan vs Esomeprazole for Early Symptom Relief in Erosive Esophagitis: A 2-Week, Double-Blind Randomized Trial Using GerdQ

Keywords
esomeprazole, vonoprazan, erosive esophagitis, GerdQ

Abstract

Introduction

This study compared the early symptom relief efficacy and safety of vonoprazan, a potassium-competitive acid blocker (P-CAB), and esomeprazole, a proton pump inhibitor (PPI), in patients with erosive esophagitis (EE). While PPIs are established treatments, P-CABs are a new option offering a faster onset of action.

Material and methods

In this multicenter, double-blind, randomized controlled trial, adults with Gastroesophageal Reflux Disease Questionnaire (GerdQ) scores ≥8 and endoscopy-confirmed EE received either vonoprazan 20 mg or esomeprazole 40 mg once daily for two weeks. The primary endpoint was complete resolution (CR) of symptoms at weeks 1 and 2 using GerdQ. Secondary endpoints included subgroup responses and safety.

Results

Among 216 participants (vonoprazan: 111; esomeprazole: 105), most had mild EE. At week 1, CR rates were 39.6% [95% CI: 31.0–48.9%] with vonoprazan and 42.9% [95% CI: 33.8–52.4%] with esomeprazole in the intention-to-treat (ITT) analysis, and 43.1% [95% CI: 33.9–52.8%] vs. 45.9% [95% CI: 36.4–55.8%] in the per-protocol (PP) analysis. At week 2, CR rates were 60.4% [95% CI: 51.1–69.0%] vs. 61.0% [95% CI: 51.4–69.7%] in ITT, and 66.3% [95% CI: 56.7–74.8%] vs. 66.0% [95% CI: 56.1–74.6%] in PP, with no significant between-group differences. Adverse events were similar, with nasopharyngitis, gastrointestinal symptoms, and headache/dizziness being the most frequent. No serious events occurred.

Conclusions

Vonoprazan and esomeprazole demonstrated similar efficacy and safety profiles for early symptom relief in patients with EE. Given these comparable outcomes, esomeprazole may represent a more economical initial option based on short-term medication costs. (ClinicalTrials.gov; NCT06720610).

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Introduction

Erosive esophagitis (EE), a subtype of gastroesophageal reflux disease (GERD), is characterized by endoscopically visible mucosal breaks in the distal esophagus caused by acid reflux.[1] Its prevalence among GERD patients varies by region. In Indonesia, reported rates range from 9.2% to 55.4%, depending on population and setting.[2,3] Clinical manifestations range from mild heartburn and regurgitation that impair quality of life to severe complications such as strictures or perforation, which may necessitate invasive treatment.[3]

Proton pump inhibitors (PPIs) are the standard therapy for EE, recommended by international guidelines, including those of the American College of Gastroenterology and the Indonesian Society of Gastroenterology, for their role in promoting mucosal healing and maintaining remission.[4,5] Among PPIs, esomeprazole 40 mg has demonstrated high efficacy in healing EE. However, PPIs have a relatively delayed onset of action, may be associated with persistent or nocturnal symptoms, and raise concerns about long-term use, including gastric atrophy and possible associations with gastric cancer.[4,6,7]

Potassium-competitive acid blockers (P-CABs), such as vonoprazan, provide more rapid and sustained acid suppression.[8] Recent trials in Japan and South Korea suggest P-CABs may offer faster symptom relief, with Oshima et al. demonstrating that vonoprazan 20 mg achieved superior symptom improvement over lansoprazole 30 mg within the first two weeks.[9]

This early 2-week response is clinically meaningful, as it correlates with higher 4-week mucosal healing rates and better treatment adherence. Early monitoring may also help identify PPI-refractory GERD, allowing prompt therapeutic adjustments to restore patient productivity and quality of life.[10]

However, direct head-to-head comparisons of vonoprazan and the potent PPI esomeprazole, specifically for early symptom relief in the first two weeks, are lacking, particularly in our population.

As an exploratory consideration, economic factors also influence treatment selection. In Indonesia, vonoprazan costs approximately United States dollars (USD) 45.5 per pack of 30 tablets compared with USD 33.8 for esomeprazole. Previous studies by Habu et al. and Li et al. have yielded mixed results; while P-CABs offer faster clinical success, some models suggest PPIs remain more cost-effective due to lower daily costs.[11,12]

Therefore, this study aimed to compare the efficacy, safety, and short-term cost of vonoprazan 20 mg versus esomeprazole 40 mg for symptom relief within the first two weeks in patients with EE.

Methods

Study Design

This multicenter, double-blind, randomized controlled trial was conducted at Cipto Mangunkusumo Hospital and four affiliated centers within the Hermina Hospital Group (Jatinegara, Bekasi, Kemayoran, and Depok, Indonesia) between December 2024 and March 2025.

Eligible participants were adults (≥18 years) diagnosed with EE, confirmed by upper gastrointestinal endoscopy, with Los Angeles (LA) grade A-D, a Gastroesophageal Reflux Disease Questionnaire (GerdQ) score ≥8, and willingness to comply with the study protocol. Exclusion criteria included allergy to PPIs/P-CABs, presence of gastric or duodenal ulcers, *Helicobacter pylori* infection, significant systemic illnesses affecting the esophagus or stomach,

esophagogastric malignancy, prior esophageal or gastric surgery, or pregnancy. Patients and the public were not involved in the design, conduct, or reporting of this trial. The study followed the registered clinical trial protocol (Identifier: NCT06720610; registered on December 3, 2024).

Diagnosis and Randomization

Endoscopic procedures were performed after a minimum of six hours of fasting using standard high-definition video endoscopes. Gastric biopsy specimens were obtained for *Helicobacter pylori* testing to ensure only *H. pylori*-negative patients were enrolled. Participants were randomized (1:1) using a computer-generated sequence by an independent staff member to receive either vonoprazan 20 mg (Vocinti®, Takeda, Japan) or esomeprazole 40 mg (S-omevell®, Novell Pharmaceutical Laboratories, Indonesia) once daily for two weeks, taken 30 minutes before breakfast; adherence was monitored through pill counts by assessors. Allocation was concealed using centralized allocation. We ensured blinding of participants, investigators, and outcome assessors; both treatments were identically encapsulated.

Symptom Assessment and Outcomes Measurement

GERD symptoms were assessed using the validated GerdQ instrument, a six-item self-administered questionnaire, with a total score of ≥8 indicating likely GERD.[5] Each item is scored from 0 to 3. It evaluates the frequency of heartburn, regurgitation, epigastric pain, nausea, sleep disturbance, and use of over-the-counter medication. No concomitant acid-suppressive medications were permitted during the study; however, any self-reported use was recorded through the GerdQ questionnaire.

Baseline evaluations included history taking and physical examination. The primary endpoint was the proportion of patients achieving complete symptom resolution (CR), defined as a score of 0 (meaning "no days") on GerdQ questions 1 (heartburn), 2 (regurgitation), 5 (nocturnal

symptoms), and 6 (use of over-the-counter medication), at weeks 1 and 2. This definition is justified as these four items specifically quantify the frequency of reflux-associated symptoms, with a total score of 0 representing the clinical threshold for a completely symptom-free state.[13] Secondary endpoints included subgroup symptom responses in patients with severe baseline symptoms (frequency of 4-7 days per week), severe EE (LA grade C/D), and the safety profile, assessed by the incidence of adverse events (AEs). AEs were defined as any unfavorable or unintended sign, symptom, or disease temporally associated with the medication, regardless of causal relationship. Overall incidence and specific symptoms were monitored across all analyses. The overall AE rate was defined as the proportion of participants experiencing at least one AE during the study period.

Sample Size Calculation

The sample size was calculated assuming a 20% absolute difference between treatments. This 20% threshold was selected as the minimum clinically important difference (MCID) for evaluating a newer therapeutic class against the established gold standard. Based on $\alpha = 0.05$ and 80% power, the required sample was 96 participants per group for week 1 and 97 for week 2. Allowing for a 10% dropout, the final target was 108 participants per group (total N = 216). The larger estimate was used to ensure adequate power across time points. No interim analyses were planned.

Statistical Analysis

Data analysis was performed using SPSS version 27.0 for Mac (IBM Corp., Armonk, NY, USA). Categorical variables are presented as frequencies and percentages. Treatment effectiveness was assessed using the Chi-square or Fisher's exact test as appropriate. Analyses were conducted for both intention-to-treat (ITT) and per-protocol (PP) populations, with $p < 0.05$ considered

statistically significant. Missing data were handled according to the ITT principle. Results are presented as frequencies and percentages with 95% confidence intervals (CI). Subgroup analyses were exploratory; no adjustment for multiplicity was performed. All randomized participants were included in the ITT analysis according to their assigned group, whereas the PP analysis included only participants who completed the study without major protocol deviations. Within-group changes in symptom outcomes over time were evaluated using a Sign Test, as proposed by Kloke and McKean (2015), in R (R Foundation for Statistical Computing, Vienna, Austria).[14] The Sign Test was applied to both ITT and PP data across time points as an exploratory robustness check of symptom improvement.

Economic Consideration

A short-term medication cost comparison was conducted as an exploratory descriptive analysis over the 2-week follow-up period. Treatment costs were derived from unit prices listed in the National Public Procurement Agency (LKPP) Electronic Catalog as of May 2025.[15,16] Economic outcomes were presented descriptively by comparing direct medication costs alongside clinical response rates within the first two weeks of treatment. Because the period was short and only direct medication costs were included, no long-term modeling or indirect cost estimation was performed. Accordingly, economic findings were interpreted descriptively.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia, Jakarta (KET-1538/UN2.F1/ETIK/PPM.00.02/2024).

Results

Baseline characteristics

Of the 216 subjects enrolled, 16 withdrew by the end of the first week, 9 from Group A and 7 from Group B, due to either lack of symptom improvement or loss to follow-up. In Group A, one subject discontinued the study early and resumed previous treatment with lansoprazole, while eight others could not be contacted. In Group B, two subjects reported persistent symptoms and opted to resume previous medications (lansoprazole or antacids), while five were lost to follow-up. During the second week, two additional subjects, one from each group, did not complete the study for similar reasons, resulting in 198 participants completing the trial. All subjects were monitored for AEs, which were managed collaboratively by the research team and physicians. After unblinding, Drug A was identified as vonoprazan and Drug B as esomeprazole. A study flow is presented in Figure 1.

Most participants were female, younger than 60 years, and non-obese. Most subjects had ceased smoking and coffee consumption within the past month, although a large proportion continued to drink tea. Only a small number of subjects had comorbid conditions. Most subjects presented with mild erosive esophagitis (EE LA grade A and B), while severe grades (EE LA grade C and D) accounted for only 4.6% of the total. Both treatment groups, vonoprazan and esomeprazole, had comparable baseline characteristics (Table 1).

Primary endpoint

Symptom improvement in both treatment groups was evaluated at weeks one and two using the GerdQ. In the ITT analysis, the proportion of patients achieving CR after one week of treatment was 39.6% [95% CI: 31.0–48.9%] in the vonoprazan group and 42.9% [95% CI: 33.8–52.4%] in the esomeprazole group (p=0.63). After two weeks, CR rates increased to 60.4% [95% CI: 51.1–69.0%] in the vonoprazan group and 61.0% [95% CI: 51.4–69.7%] in the esomeprazole group

(p=0.93). In the PP analysis, the CR rate after one week was 43.1% [95% CI: 33.9–52.8%] for the vonoprazan group and 45.9% [95% CI: 36.4–55.8%] for the esomeprazole group (p=0.69). After two weeks, CR rates further increased to 66.3% [95% CI: 56.7–74.8%] in the vonoprazan group and 66.0% [95% CI: 56.1–74.6%] in the esomeprazole group (p=0.96) (Figure 2).

Secondary Endpoints

Severe Symptom Subgroups

To evaluate the clinical response in patients with high baseline symptom burdens, subgroup analyses were performed. These exploratory findings are intended to be hypothesis-generating, given the limited sample sizes in specific cohorts.

Among patients with severe heartburn (n=79), vonoprazan showed a numerical trend toward a higher CR rate than esomeprazole at week 1 (n=24/44, 54.5% [95% CI: 40.1–68.2%] vs. n=13/35, 37.1% [95% CI: 23.2–53.7%]) and week 2 (n=29/44, 65.9% [95% CI: 51.1–78.1%] vs. n=22/35, 62.9% [95% CI: 46.3–76.8%]). A similar trend favoring vonoprazan was observed for severe regurgitation (n=108) at week 1 (n=26/58, 44.8% [95% CI: 32.7–57.6%] vs. n=20/50, 40.0% [95% CI: 27.6–53.8%]) and week 2 (n=41/58, 70.7% [95% CI: 58.0–80.9%] vs. n=33/50, 66.0% [95% CI: 52.1–77.6%]). Conversely, resolution of severe nocturnal symptoms (n=110) was comparable between groups, with vonoprazan showing slightly lower numerical CR rates at week 1 (n=43/63, 68.3% [95% CI: 56.0–78.4%] vs. n=35/47, 74.5% [95% CI: 60.5–84.8%]) and week 2 (n=52/63, 82.5% [95% CI: 71.5–90.0%] vs. n=41/47, 87.2% [95% CI: 74.8–94.0%]).

In the subgroup of patients experiencing combined severe symptoms (n=22), vonoprazan achieved a higher numerical CR rate at week 1 (n=4/11, 36.4% [95% CI: 15.0–64.8%]) compared with esomeprazole (n=2/11, 18.2% [95% CI: 5.1–47.7%]). By week 2, resolution rates remained comparable between the groups, with 36.4% [95% CI: 15.0–64.8%] (n=4/11) in the

vonoprazan arm and 45.5% [95% CI: 21.3–72.0%] (n=5/11) in the esomeprazole arm. These results are summarized in Figure 3A.

Severe Erosive Esophagitis Subgroup

Correlation analysis between baseline GerdQ and LA severity revealed a very weak, non-significant relationship (Spearman's ρ=0.064,p=0.348). This suggests that in this study population, subjective symptoms and objective mucosal damage are independent clinical markers.

Among patients with endoscopically confirmed severe EE (n = 10), vonoprazan showed a more rapid clinical response. At week 1, the CR rate was 42.9% [95% CI: 15.8–75.0%] (n=3/7) in the vonoprazan group compared with 0% [95% CI: 0.0–56.1%] (n=0/3) in the esomeprazole group. By week 2, resolution rates remained numerically higher for vonoprazan (n=3/7, 42.9% [95% CI: 15.8–75.0%]) than for esomeprazole (n=1/3, 33.3% [95% CI: 6.1–79.2%]) (Figure 3B).

Adverse Events

The AEs identified in this study included nasopharyngitis, diarrhea, lower back pain, constipation, dizziness/headache, dysgeusia, abdominal bloating, and abdominal pain. Both treatment groups showed similar proportions of AEs. No serious AEs were observed throughout the study. A complete summary of all reported AEs is presented in Table 2.

The Sign Test confirmed statistically significant within-group symptom improvement. Both vonoprazan and esomeprazole demonstrated statistically significant clinical responses across all analytical approaches (ITT and PP) at week 1, with p-values of 0.0072 and 0.0001, respectively, and both achieved $p < 0.0001$ at week 2 in the overall population. In the subgroup analysis on severe EE, both treatments maintained identical statistical significance patterns, suggesting

robust treatment despite smaller sample sizes (n=10). Given that both treatments demonstrated symptom improvement with no significant between-group differences, a descriptive cost comparison was performed to contextualize treatment choice based on medication acquisition cost.

Discussion

The study maintained an acceptable dropout rate (<10%) and exceeded the required sample size. The 4.6% prevalence of severe EE (LA grade C/D) is significantly lower than the 24–34% reported in trials by Ashida et al., Xiao et al., Laine et al., and Sakurai et al.[17–20], but aligns with other Asian studies reporting rates between 0% and 6%.[21,22] This discrepancy is likely driven by inclusion criteria; for instance, the study by Ashida et al. specifically capped mild cases, and the study by Sakurai et al. required high baseline symptom scores.[17,23] Our findings also align with regional data from South Korea, Taiwan, and Indonesian cohorts (0–6%), suggesting that this study population reflects the real-world distribution of severe EE in the region.[24–27]

This study demonstrates that vonoprazan and esomeprazole provide comparable clinical efficacy in achieving symptom CR at weeks 1 and 2 in patients with EE primarily characterized by mild mucosal damage, in both ITT and PP analyses. The similar outcomes can be partly explained by the pharmacodynamic profiles of both agents. Esomeprazole is a prodrug that is activated in an acidic environment and gradually reaches maximal effect after 3–5 days, whereas vonoprazan inhibits H+/K+-ATPase without requiring acid activation, providing faster onset and more sustained action.[28,29] Vonoprazan rapidly achieves a high pH > 4 holding time ratio (HTR), which may favor earlier symptom improvement. However, in a cohort dominated by mild EE, esomeprazole may already achieve sufficient acid suppression to reduce esophageal acid

exposure below the symptomatic threshold, limiting the clinical advantage of stronger early pH control.[30] Additionally, although PPIs are metabolized by CYP2C19, which can reduce acid suppression in rapid metabolizers, esomeprazole is less affected than older PPIs.[31] The higher prevalence of intermediate metabolizers in Asian populations may further support adequate acid suppression.[32] Together, these factors may explain the comparable early symptom resolution between treatments.

To further explore treatment response, we performed exploratory, hypothesis-generating subgroup analyses in patients with high baseline symptom burden. Severe heartburn was observed in 79 out of 216 subjects (36.6%), with vonoprazan showing a numerically higher proportion of complete resolution compared with esomeprazole after one (54.5% vs. 37.1%, p=0.12) and two weeks (65.9% vs. 62.9%, p=0.77) (Figure 3). The observed gap in symptom resolution during the first week may reflect vonoprazan's rapid acid suppression; however, by the second week, both treatments achieved comparable therapeutic outcomes, which may suggest that both therapies achieved adequate control within the early treatment window.[8,33]

Severe regurgitation was reported in 108 subjects (50.0%), with only marginal differences in resolution rates between vonoprazan and esomeprazole at both time points. The complex mechanisms of regurgitation, reflux of gastric contents other than acid, and lower esophageal sphincter dysfunction limit the impact of acid suppression alone.[8,33]

Nocturnal symptoms were severe in 110 subjects (50.9%). While vonoprazan's longer duration of action through CYP3A4 metabolism could potentially offer advantages, its efficacy was comparable to esomeprazole, which also provides stable acid suppression. Non-pharmacological measures, such as elevated sleeping positions and dietary adjustments, likely contributed to symptom improvement in both groups.[22,34]

For patients with severe EE (n=10, 4.6%), vonoprazan demonstrated higher resolution rates, particularly in the first week. These findings align with previous studies highlighting the rapid onset of P-CABs and stronger acid inhibition compared with PPIs, particularly in the early phases of treatment. Differences narrowed by week 2, likely due to both drugs achieving sufficient acid suppression.[8,33]

The greater variability in early symptom resolution in severe cases may reflect the relationship between disease severity and acid exposure duration. Severe EE is associated with prolonged acid exposure, making the faster onset of vonoprazan more apparent.[35] In contrast, in mild EE, where acid exposure is less pronounced, the therapeutic effects of vonoprazan and esomeprazole appear similar. These subgroup patterns are consistent with the pharmacodynamic profile of vonoprazan, particularly in early symptom resolution.[36] However, these findings should be considered hypothesis-generating, as they are based on small numbers and non-significant differences.

Adverse events reported were mild and comparable between groups, with no serious adverse events observed. These findings align with studies by Lee et al., Cho et al., and Tack et al., which also involved a low proportion of patients with severe EE, similar to the 4.6% observed in this study.[21,22,37] In contrast, studies by Ashida et al., Xiao et al., Laine et al., and a sub-analysis by Sakurai et al. reported higher proportions of severe EE and found vonoprazan to be superior. Furthermore, while Lee et al. and Tack et al. used esomeprazole as the comparator, Ashida et al., Xiao et al., and Laine et al. used lansoprazole.[17–19,23] Meta-analysis by Li et al. suggested that esomeprazole is slightly more effective than lansoprazole and other PPIs, and a network meta-analysis by Zhuang et al. found esomeprazole to be the only PPI comparable to vonoprazan in treating severe EE.[38,39]

During subject monitoring, AEs from both treatments were assessed. Nasopharyngitis was the most frequently reported event, followed by headache, diarrhea, and constipation. This is consistent with the study by Ashida et al., which also identified nasopharyngitis, diarrhea, and constipation as the most common AEs. The overall incidence of AEs in this study was lower than that reported by Ashida, and there was no statistically significant difference in adverse events between the two treatment groups.[17]

Our additional statistical robustness check confirms that both treatments are effective, with no statistically significant difference in efficacy between vonoprazan and esomeprazole. In the week-1 ITT and PP populations, esomeprazole showed slightly higher rates of complete resolution, though not statistically significant. Considering the cost, the retail price (Harga Netto Apotek/HNA) in Indonesia in 2024 for a pack of 30 tablets is IDR 740,000 for vonoprazan 20 mg and IDR 550,000 for esomeprazole. Using an approximate exchange rate of 1 USD = 16,271 IDR, this corresponds to about USD 45.5 for vonoprazan and USD 33.8 for esomeprazole. Thus, the cost per pack of esomeprazole is approximately 75% of the cost of vonoprazan, while the rates of CR were nearly identical in the overall EE population, supporting esomeprazole as the more economically favorable option for general use.

However, in the severe EE subgroup, vonoprazan appeared to be more effective, despite the small sample size. Therefore, vonoprazan may offer greater clinical value in severe EE, although this observation should be considered exploratory and requires confirmation in larger studies with longer follow-up.

The study has several limitations. First, most patients had mild EE, and the small proportion with severe EE (4.6%) limited the power and precision of subgroup analyses. Second, the short two-week observation period focused on early symptom relief. Therefore, long-term mucosal healing,

recurrence outcomes, and the long-term effect of these two drugs could not be evaluated. Additionally, the study population consisted primarily of Indonesian patients with mild EE and a low comorbidity burden, which may limit the generalizability of the findings to populations with a higher prevalence of severe EE, obesity, or comorbidities.

Conclusion

Vonoprazan and esomeprazole showed comparable efficacy and safety for early symptom relief in patients with EE after one and two weeks. In this trial, an exploratory 2-week comparison of drug acquisition costs suggested that esomeprazole may be the more economical initial option based on short-term medication costs. Further studies are needed to evaluate their relative benefits in specific subgroups, particularly those with severe EE.

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Study Design

- Adults with EE
- GerdQ ≥8

→ Randomization

- Vonoprazan 20 mg n=111
- Esomeprazole 40 mg n=105

2 weeks, double-blind RCT
evaluated by GerdQ in one and two weeks

Primary Endpoint

Proportion of patients achieving **complete symptom resolution**, defined as a score of "no days" on GerdQ 1 (heartburn), 2 (regurgitation), 5 (sleep disturbance), and 6 (use of OTC medication)

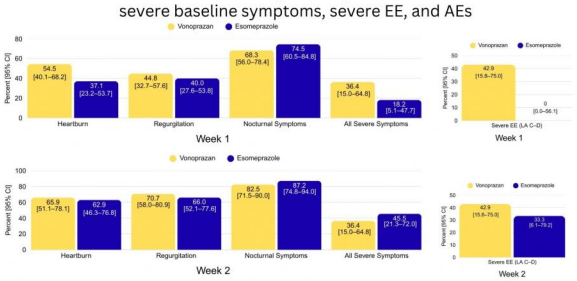
Week 1: 39.6% vs 42.9% (ITT) — p = 0.63
Week 2: 60.4% vs 61.0% (ITT) — p = 0.93

Conclusions

Vonoprazan and esomeprazole **provided similar early symptom relief and safety** in EE, but esomeprazole may represent a more economically favorable initial treatment option in this setting.

Secondary Endpoint

severe baseline symptoms, severe EE, and AEs



Safety: Similar AE profile; no serious AEs
Cost comparison: Vonoprazan ~USD 45.5 vs Esomeprazole ~USD 33.8 per box

Table 1. Baseline Characteristics of Patients with Erosive Esophagitis in Vonoprazan vs. Esomeprazole Groups

Characteristics	Total (n=216)	Treatment Groups		*P* value	Test
		Vonoprazan (n= 111)	Esomeprazole (n= 105)		
Sex, n (%) [95% CI]				0.014	χ^2
Female	145 (67.1) [60.6–73.0]	66 (59.5) [50.2–68.1]	79 (75.2) [66.2–82.5]		
Male	71 (32.9) [27.0–39.4]	45 (40.5) [31.9–49.8]	26 (24.8) [17.5–33.8]		
Age, n (%) [95% CI]				0.370	χ^2
< 60 years	176 (81.5) [75.8–86.1]	93 (83.8) [75.8–89.5]	83 (79) [70.2–85.9]		
>= 60 years	40 (18.5) [13.9–24.2]	18 (16.2) [10.5–24.2]	22 (21) [14.1–29.8]		
Obesity, n (%) [95% CI]				0.112	χ^2
Non-obese	126 (58.3) [51.7–64.7]	59 (53.2) [43.9–62.2]	67 (63.8) [54.2–72.4]		
Obesity	90 (41.7) [35.3–48.3]	52 (46.8) [37.8–56.1]	38 (36.2) [27.6–45.8]		
Smoking habit, n (%) [95% CI]				0.220	χ^2
Non-smoker	201 (93.1) [88.9–95.7]	101 (91.0) [84.2–95.0]	100 (95.2) [89.3–97.9]		
Smoker	15 (6.9) [4.3–11.1]	10 (9.0) [5.0–15.8]	5 (4.8) [2.1–10.7]		
Alcohol consumption, n (%) [95% CI]				0.358	Fisher Exact
No	212 (98.1) [95.3–99.3]	110 (99.1) [95.1–99.8]	102 (97.1) [91.9–99.0]		
Yes	4 (1.9) [0.7–4.7]	1 (0.9) [0.2–4.9]	3 (2.9) [1.0–8.1]		
Coffee consumption, n (%) [95% CI]				0.442	χ^2
No.	128 (59.3) [52.6–65.6]	63 (56.8) [47.5–65.7]	65 (61.9) [52.3–70.6]		
Yes	88 (40.7) [34.4–47.4]	48 (43.2) [34.3–52.5]	40 (38.1) [29.4–47.7]		
Tea consumption, n (%) [95% CI]				0.561	χ^2
No.	74 (34.3) [28.3–40.8]	36 (32.4) [24.4–41.6]	38 (36.2) [27.6–45.8]		
Yes	142 (65.7) [59.2–71.7]	75 (67.6) [58.4–75.6]	67 (63.8) [54.2–72.4]		
Comorbidities, n (%) [95% CI]					
Type 2 diabetes mellitus				0.870	χ^2
No	186 (86.1) [80.9–90.1]	96 (86.5) [78.9–91.7]	90 (85.7) [77.8–91.1]		
Yes	30 (13.9) [9.9–19.1]	15 (13.5) [8.3–21.1]	15 (14.3) [8.9–22.2]		
Hypertension				0.362	χ^2

No	150 (69.4) [63.0–75.2]	74 (66.7) [57.4–74.8]	76 (72.4) [63.2–80.0]		
Yes	66 (30.6) [24.8–37.0]	37 (33.3) [25.2–42.6]	29 (27.6) [20.0–36.8]		
Coronary heart disease				0.755	χ^2
No	194 (89.8) [85.1–93.2]	99 (89.2) [82.1–93.7]	95 (90.5) [83.3–94.8]		
Yes	22 (10.2) [6.8–14.9]	12 (10.8) [6.3–17.9]	10 (9.5) [5.2–16.7]		
Asthma				0.940	Fisher Exact
No	206 (95.4) [91.7–97.5]	106 (95.5) [89.8–98.1]	100 (95.2) [89.3–97.9]		
Yes	10 (4.6) [2.5–8.3]	5 (4.5) [1.9–10.2]	5 (4.8) [2.1–10.7]		
Stroke				>0.999	Fisher Exact
No	214 (99.1) [96.7–99.7]	110 (99.1) [95.1–99.8]	104 (99.0) [94.8–99.8]		
Yes	2 (0.9) [0.3–3.3]	1 (0.9) [0.2–4.9]	1 (1.0) [0.2–5.2]		
Malignancy				>0.999	Fisher Exact
No	214 (99.1) [96.7–99.7]	110 (99.1) [95.1–99.8]	104 (99.1) [94.8–99.8]		
Yes	2 (0.9) [0.3–3.3]	1 (0.9) [0.2–4.9]	1 (1.0) [0.2–5.2]		
Autoimmune disease				0.486	Fisher Exact
No	215 (99.5) [97.4–99.9]	111 (100.0) [96.7–100.0]	104 (99.0) [94.8–99.8]		
Yes	1 (0.5) [0.1–2.6]	0 (0.0) [0.0–3.3]	1 (1.0) [0.2–5.2]		
Sample collection locations, n (%) [95% CI]				0.602	χ^2
Hermina Jatinegara Hospital	93 (43.1) [36.6–49.7]	49 (44.1) [35.2–53.4]	44 (41.9) [32.9–51.5]		
Hermina Kemayoran Hospital	20 (9.3) [6.1–13.9]	13 (11.7) [7.0–19.0]	7 (6.7) [3.3–13.1]		
Hermina Depok Hospital	24 (11.1) [7.6–16.0]	11 (9.9) [5.6–16.9]	13 (12.4) [7.4–20.0]		
Hermina Bekasi Hospital	45 (20.8) [16.0–26.7]	20 (18.0) [11.9–26.2]	25 (23.8) [16.7–32.7]		
RS Cipto Mangunkusumo	34 (15.7) [11.5–21.2]	18 (16.2) [10.5–24.1]	16 (15.2) [9.6–23.3]		
Severity of erosive esophagitis, n (%) [95% CI]				0.708	Fisher Exact
LA *grade A*	174 (80.6) [74.8–85.3]	88 (79.3) [70.8–85.8]	86 (81.9) [73.4–88.1]		
LA *grade B*	32 (14.8) [10.7–20.2]	16 (14.4) [9.1–22.1]	16 (15.2) [9.6–23.3]		
LA *grade C*	9 (4.2) [2.2–7.7]	6 (5.4) [2.5–11.3]	3 (2.9) [1.0–8.1]		
LA *grade D*	1 (0.5)	1 (0.9)	0 (0.0)		

	[0.1–2.6]	[0.2–4.9]	[0.0–3.5]		
GerdQ Baseline, median (IQR)	9 (3)	10 (4)	9 (3)	0.073	U

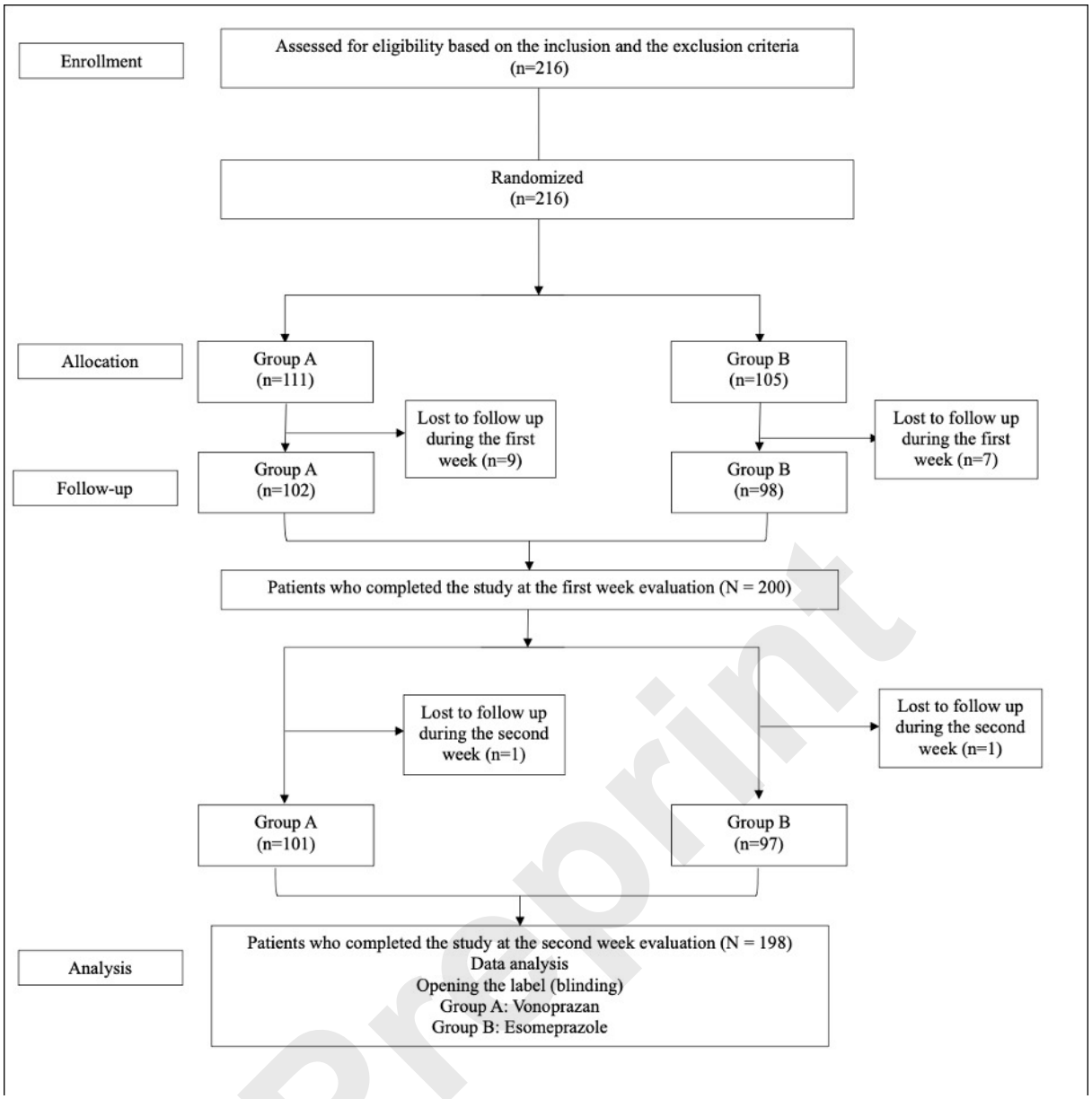
CI, confidence interval; IQR, interquartile range; LA, Los Angeles classification; GerdQ, Gastroesophageal Reflux Disease Questionnaire.

Table 2. Comparison of Adverse Events in Vonoprazan vs. Esomeprazole Groups

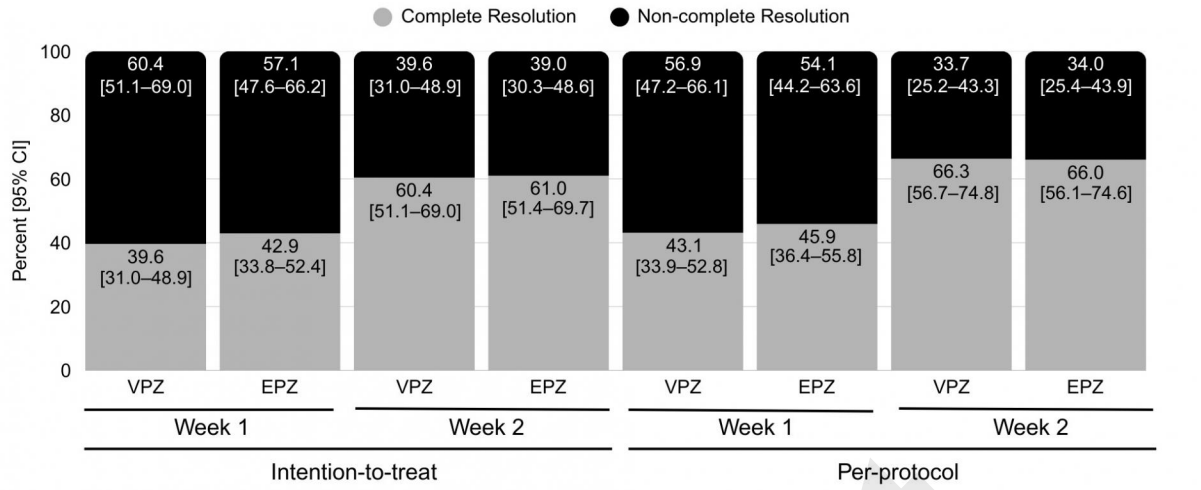
Adverse Events	**Vonoprazan (n=111)** **n (%) [95% CI]**	**Esomeprazole (n=105)** **n (%) [95% CI]**	***P* value**	**Test**
Overall AEs	23 (20.7) [13.6–29.5]	22 (21.0) [13.7–29.9]	0.967	χ^2
Nasopharyngitis			0.111	Fisher Exact
No	110 (99.1) [95.1–99.8]	100 (95.2) [89.3–97.9]		
Yes	1 (0.9) [0.2–4.9]	5 (4.8) [2.1–10.7]		
Diarrhea			0.749	Fisher Exact
No	105 (94.6) [88.7–97.5]	101 (96.2) [90.6–98.5]		
Yes	6 (5.4) [2.5–11.3]	4 (3.8) [1.5–9.4]		
Lower back pain			0.622	Fisher Exact
No	108 (97.3) [92.4–99.1]	104 (99.0) [94.8–99.8]		
Yes	3 (2.7) [0.9–7.6]	1 (1.0) [0.2–5.2]		
Constipation			0.686	χ^2
No	106 (95.5) [89.9–98.0]	99 (94.3) [88.1–97.4]		
Yes	5 (4.5) [1.9–10.2]	6 (5.7) [2.6–11.9]		
Dizziness/headache			0.830	χ^2
No	105 (94.6) [88.7–97.5]	100 (95.2) [89.3–97.9]		
Yes	6 (5.4) [2.5–11.3]	5 (4.8) [2.1–10.7]		
Dysgeusia			>0.999	Fisher Exact
No	109 (98.2) [93.7–99.5]	103 (98.1) [93.3–99.5]		
Yes	2 (1.8) [0.5–6.3]	2 (1.9) [0.5–6.7]		

Abdominal bloating			0.358	Fisher Exact
No	110 (99.1) [95.1–99.8]	102 (97.1) [91.9–99.0]		
Yes	1 (0.9) [0.2–4.9]	3 (2.9) [1.0–8.1]		
Abdominal pain			>0.999	Fisher Exact
No	110 (99.1) [95.1–99.8]	105 (100.0) [96.5–100.0]		
Yes	1 (0.9) [0.2–4.9]	0 (0.0) [0.0–3.5]		

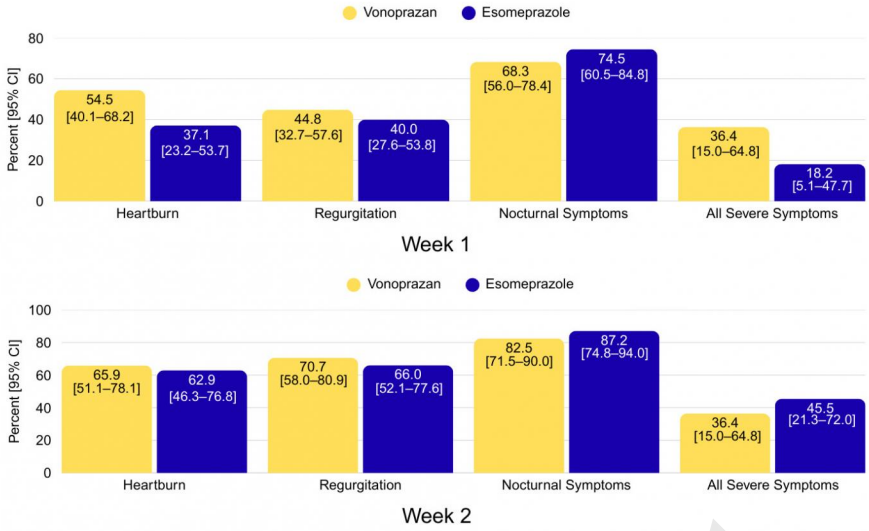
AEs, adverse events; CI, confidence interval.



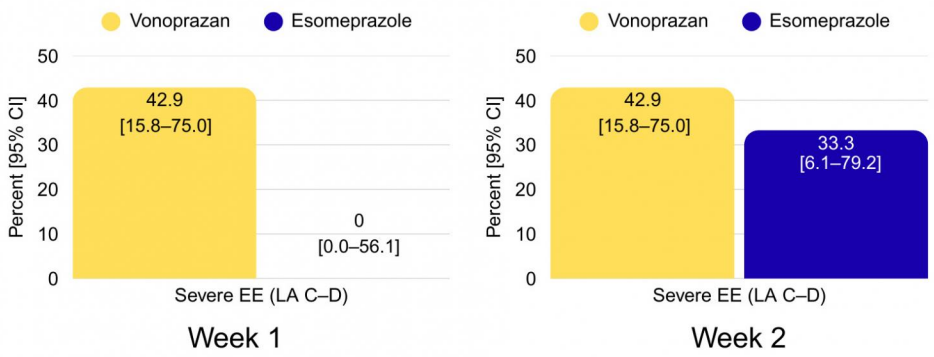
CONSORT Flow Chart of Participants.



Symptom Resolution based on GerdQ Responses at Week 1 and Week 2. VPZ: vonoprazan, EPZ: esomeprazole.



Symptom Resolution by Severe Symptom Subgroups at Week 1 and Week 2. EE: erosive esophagitis, LA: Los Angeles



Symptom Resolution by Severe Erosive Esophagitis Subgroup at Week 1 and Week 2. EE: erosive esophagitis, LA: Los Angeles