SYSTEMATIC REVIEW

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Efficacy of Vonoprazan with Amoxicillin as the First Line Therapy for *Helicobacter pylori* Eradication in Asian Population: A Systematic Review, Meta-Analysis, and Meta-Regression of Clinical Studies

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ABSTRACT

Background & Aims: *Helicobacter pylori* (*H. pylori*) infection remains a major public health problem in Asia, with high prevalence and increasing therapeutic resistance. Vonoprazan (VPZ), a potassium-competitive acid blocker, combined with amoxicillin is thought to improve eradication rates in first-line therapy. This study evaluated the efficacy of VPZ with amoxicillin as first-line therapy for *H. pylori* eradication in an Asian population.

Methods: A systematic review and meta-analysis of clinical studies was conducted according to PRISMA guidelines. A literature search was conducted in PubMed and ScienceDirect through September 2025. Data related to the eradication rate (ER) of VPZ-amoxicillin and the comparison of VPZ-amoxicillin eradication with proton pump inhibitors (PPIs) were extracted and analyzed. Data were analyzed using a random-effects model with the main effect sizes being ER and risk difference (RD), as well as meta-regression against age and body mass index (BMI). Data analysis was performed using RevMan 5.4 and R software.

Results: This study included 22 clinical studies with 32 comparisons involving 7,498 participants. The VPZ-amoxicillin combination in dual, triple, and quadruple therapy regimens had ERs of 0.92 (95%CI: 0.90-0.95); 0.93 (95%CI: 0.91-0.95); and 0.96 (95%CI: 0.93-0.99), respectively, for a total eradication rate of 0.94 (95%CI: 0.91-0.96). Comparison with PPIs showed a risk difference of 0.06 (95%CI: 0.02-0.09) overall and 0.03 (95%CI: -0.02-0.08); 0.07 (95%CI: 0.02-0.12) and 0.04 (95%CI: 0-0.07) in dual, triple, and quadruple therapy, respectively. Meta-regression showed that age (p=0.006) influenced therapy effectiveness, but BMI (p=0.411) did not.

Conclusion: Vonoprazan with amoxicillin is effective as first-line therapy for *H. pylori* eradication in the Asian population.

Key words: amoxicillin – Asian population – *Helicobacter pylori* – vonoprazan.

Abbreviations: BMI: body mass index; ER: eradication rate; *H. pylori: Helicobacter pylori*; PPI: proton pump inhibitor; RD: risk difference.

INTRODUCTION

Helicobacter pylori (*H. pylori*) infection is one of the most common chronic infectious diseases worldwide, with a global prevalence reaching over 50% of the population. This infection has an uneven geographic distribution, with the highest incidence rates recorded in East and Southeast Asia [1, 2]. Countries such as Japan, China, and South Korea report prevalence rates between 40–70%, while some Southeast Asian countries such as Vietnam, Thailand, and Indonesia show infection rates that can even exceed 75% in the adult population [3, 4]. This disease burden is significant because *H. pylori* plays a role in the pathogenesis of various gastrointestinal disorders such as chronic gastritis, peptic ulcer disease, mucosa associate lymphoid tissue (MALT) lymphoma, and gastric carcinoma, which collectively contribute to high morbidity and mortality in the Asian region [5, 6].

The urgency of *H. pylori* eradication is heightened by the World Health Organization (WHO) classification of this bacterium as a class I carcinogen for gastric cancer. In Asia, approximately 60–80% of gastric cancer cases are directly linked to *H. pylori* infection, particularly the more virulent cagA-positive subtype, which is more prevalent in Asian

populations than in other regions. Furthermore, the economic burden of *H. pylori*-related disease is significant, encompassing long-term treatment costs and lost productivity. Effective, affordable, and regionally tailored eradication efforts are a priority in public health strategies, particularly in regions with high prevalence and rapidly increasing antibiotic resistance [7, 8].

The most common first-line therapy used over the past few decades has been triple therapy based on proton pump inhibitors (PPIs) in combination with two antibiotics, usually amoxicillin and clarithromycin. However, the effectiveness of this regimen has steadily declined over the past decade, primarily due to the rise of clarithromycin resistance, which now exceeds 20% in most Asian countries. Furthermore, PPI effectiveness is highly dependent on a patient's genetic metabolic factors, particularly CYP2C19 variants, which influence bioavailability and gastric acid suppression potential. In Asian populations, where the proportion of rapid metabolizers is relatively high, the ability of PPIs to maintain optimal intragastric pH is reduced, thus reducing antibiotic stability and effectiveness [9-11].

Vonoprazan (VPZ), a potassium-competitive acid blocker (PCAB), was developed as an alternative to PPIs with a more rapid, potent, and stable inhibition of gastric acid secretion. Vonoprazan's mechanism of action does not depend on acid activation or CYP2C19 enzymatic metabolism, making it more consistent in maintaining a neutral gastric pH than conventional PPIs [12-14]. This more stable pH is crucial for enhancing the optimal bactericidal activity of amoxicillin at a neutral pH and reducing eradication failure due to gastric acid fluctuations. Several clinical trials in Asia have shown that the VPZ-amoxicillin dual therapy regimen is comparable in effectiveness to, and even exceeds, PPI-based triple therapy regimens, with eradication rates exceeding 90% in most studies [15, 16]. In addition to its effectiveness, the VPZ-based regimen offers a good safety and tolerability profile, with a lower incidence of gastrointestinal side effects than combinations with clarithromycin or metronidazole. This makes the VPZ–amoxicillin regimen an attractive candidate for new first-line therapy in Asia, where antibiotic resistance is high. However, significant differences in results remain between studies, possibly due to variations in therapy duration (7–14 days), amoxicillin dosage, patient age, body mass index (BMI), and comparison with different PPIs (omeprazole, lansoprazole, rabeprazole) [17, 18].

Although several previous meta-analyses have evaluated the effectiveness of VPZ as an *H. pylori* eradication therapy, most have not focused specifically on Asian populations, even though this region has different antibiotic resistance patterns, genetic characteristics of drug metabolism, and clinical profiles compared to other regions. In addition, there has been no comprehensive review that simultaneously compared dual, triple, and quadruple VPZ–amoxicillin regimens and included meta-regression analyzes to evaluate the influence of demographic factors such as age and body mass index. A number of recent randomized clinical trials from the period 2022–2025 have also not been included in previous meta-analyses, so a synthesis of the latest evidence is needed to produce effectiveness estimates that are more accurate and relevant to current clinical practice. Moreover, there is no meta-regression analysis that is done on the previous literature. Based on this background, a systematic review and meta-analysis was conducted to objectively and comprehensively assess the effectiveness of the VPZ–amoxicillin combination as a first-line therapy for *H. pylori* eradication in Asian populations. This analysis aims to synthesize the latest evidence from published clinical studies, including comparisons with PPI-based regimens, and assess the potential impact of demographic factors such as age and BMI on treatment efficacy through meta-regression analysis.

METHODS

Study Design and Protocol

This study was structured as a systematic review and meta-analysis based on the latest version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles. The review protocol was prospectively registered with PROSPERO to ensure transparency and avoid duplication of topics under ID CRD420251155137. All research steps, from literature search, study selection, data extraction, and statistical analysis, were conducted sequentially using an evidence-based approach, as shown in Fig 1.

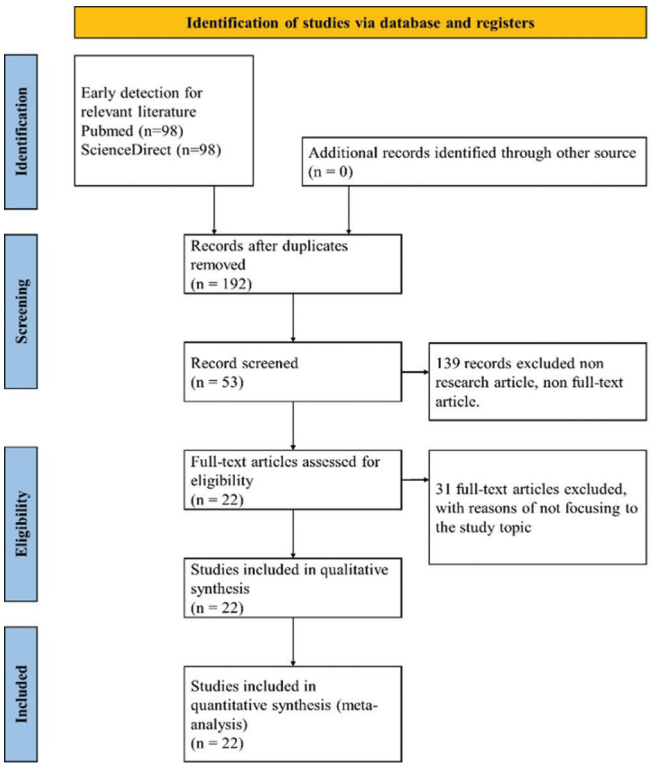

Fig. 1. PRISMA flowchart.

Literature Search Strategy

A systematic literature search was conducted in PubMed and ScienceDirect databases. The search timeframe included publications from the beginning of data collection to September 2025, without language restrictions, with a focus on studies involving Asian populations. Keywords were developed through a combination of Medical Subject Headings (MeSH)

and free terms, including: ("Vonoprazan") AND ("Amoxicillin") AND ("*Helicobacter pylori*" OR "*H. pylori*") AND (Asia OR Asian OR Japan OR China OR Korea OR India OR Thailand) AND ("eradication" OR "therapy" OR "treatment") AND ("first line" OR "initial therapy"). The search strategy was adapted to the format of each database and expanded by manual searches of the bibliographies of relevant articles and previous reviews.

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria: (1) clinical studies; (2) an Asian adult population with *H. pylori* infection confirmed by a breath urease test, histology, or stool antigen test; (3) an intervention involving a combination of VPZ and amoxicillin as first-line therapy; and (4) a primary outcome of bacterial eradication rates after therapy. Studies with case reports and narrative reviews were excluded from the analysis.

Extraction Procedure and Quality Assessment

Two independent researchers conducted article selection and data extraction using a standardized form. Data collected included baseline participant characteristics, type and dose of therapy, type and dose of comparator, duration of therapy, and the proportion of successful therapy outcomes. If there were discrepancies in assessments, the final decision was reached through consensus or discussion. The methodological quality of each clinical studies was evaluated using the Risk of Bias (RoB 2) criteria developed by the Cochrane Collaboration, which encompasses six main domains: randomization process, deviation from intervention, missing data, outcome measurement, reporting of results, and overall assessment.

Statistical Analysis

Data were analyzed using Review Manager (RevMan) and R software. Eradication rates were expressed as proportions and analyzed using fixed or random-effects models, accounting for inter-study variation. Heterogeneity was evaluated using the Cochrane Q test and the I^2 index, with an I^2 value >50% indicating significant heterogeneity. Subgroup analyses were performed based on duration of therapy, amoxicillin dose, and comparator. Potential publication bias was analyzed using funnel plots and Egger's test. A mixed linear model-based meta-regression was then conducted to explore the relationship between eradication effectiveness and covariate factors.

RESULT

Characteristic of Included Studies

This systematic review and meta-analysis included 22 clinical studies with 32 comparisons involving 7,498 patients undergoing *H. pylori* eradication therapy using a VPZ and amoxicillin-based regimen. All studies were conducted in Asia, with the following geographic distribution, China (12 studies), Japan (8 studies), South Korea (3 studies), Taiwan (2 studies), and one study each from Thailand, Hong Kong, and Pakistan. All studies were clinical studies, with the intervention group using a VPZ-amoxicillin combination in dual, triple, or quadruple therapy, while the comparison group used PPIs therapy such as omeprazole, lansoprazole, rabeprazole, or esomeprazole. Several studies used bismuth-based regimens as active controls as seen in Supplementary Table I [15, 16, 19-37].

The duration of therapy used varies between 7, 10, and 14 days, with 14 days being the most common regimen in recent studies. Amoxicillin doses range from 750 mg to 1000 mg per dose, given two or three times daily. Most studies used vonoprazan 20 mg twice daily, while additional antibiotics such as clarithromycin, metronidazole, or furazolidone were used in triple and quadruple regimens. Of the total studies, 11 evaluated dual therapy (VPZ-amoxicillin), 10 evaluated triple therapy (VPZ+amoxicillin+clarithromycin), and 7 evaluated quadruple therapy involving the addition of bismuth or probiotics.

Risk of Bias Analysis

The results of the risk of bias analysis using the RoB2 tools are shown in Supplementary file, Fig. 1. The figure shows that of all studies, 9 studies have a low risk of bias, 9 studies have a risk of bias that needs to be considered (some concern), and 4 studies have a high risk of bias.

Efficacy of VPZ-Amoxicillin First-Line Dual Therapy

An analysis was conducted to evaluate the effectiveness of VPZ-amoxicillin first-line dual therapy on eradicating *H. pylori*. Fig. 2A analyzes the subgroups based on therapy duration. These results indicate that dual therapy with a duration of 7 days, 10 days, and 14 days each had ERs of 0.77 (95%CI: 0.65–0.90), 0.86 (95%CI: 0.78–0.94), and 0.94 (95%CI: 0.91–0.96), respectively. These results indicate that therapy with a duration of 14 days provided the best eradication outcome. Fig. 2B below evaluates the effectiveness of VPZ-amoxicillin first-line dual therapy on eradicating *H. pylori* based on amoxicillin dose. These results show that the eradication rate for amoxicillin administration at a dose of <3000 mg/day compared to >3000 mg/day was 0.92 (95%CI: 0.88–0.95) and 0.93 (95%CI: 0.90–0.96), respectively, indicating a slight superiority in administering amoxicillin at a higher dose.

Efficacy of VPZ-Amoxicillin First-Line Triple Therapy

The results of data analysis on the effectiveness of VPZ-amoxicillin first-line triple therapy in eradicating *H. pylori* based on treatment duration are shown in Fig. 3A below. The results of the data analysis indicate that the duration of therapy of 7 days, 10 days, and 4 days in this triple therapy regimen has an ER value of 0.93 (95%CI: 0.89-0.97), 0.90 (95%CI: 0.86-0.94) and 0.95 (95%CI: 0.93-0.97), respectively, indicating that the duration of 14 days provides the best clinical outcome. Further analysis was also conducted to evaluate the effect of amoxicillin dosage on the effectiveness of therapy, as shown in Fig. 3B. The data analysis showed that amoxicillin with a dosage of <2000 mg/day compared to >= 2000 mg/day had ERs of 0.94 (95%CI: 0.91–0.96) and 0.93 (95%CI: 0.90–0.96), respectively. This indicates that there is only a slight difference in eradication rates between these two regimens.

Efficacy of VPZ-Amoxicillin First-Line Quadruple Therapy

The results of the data analysis showed that the quadruple therapy regimen with a duration of administration of 10 days

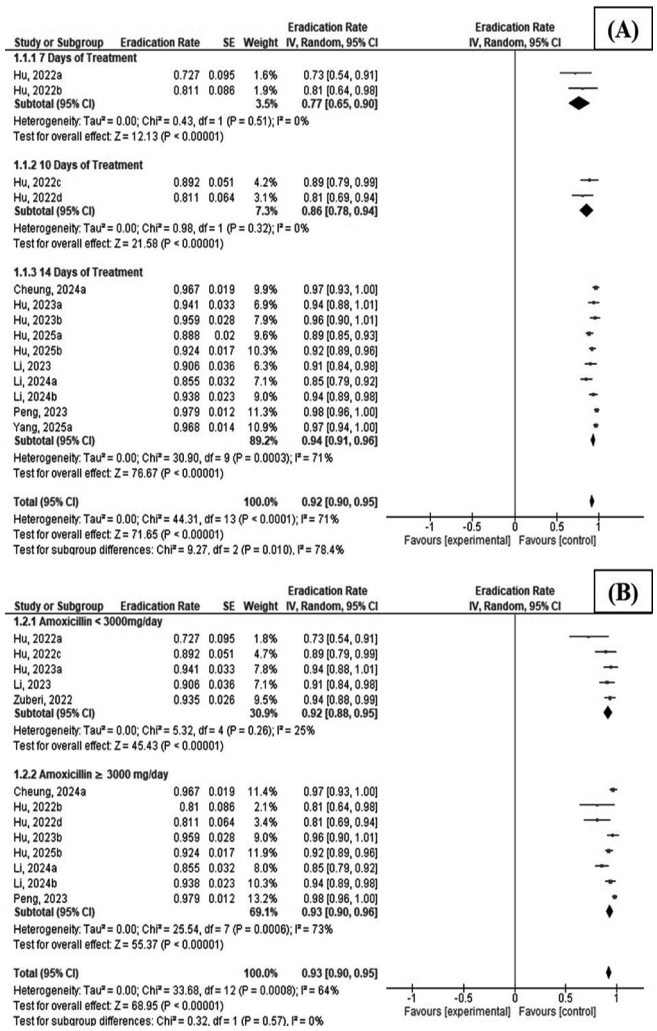

Fig. 2. Forest plot analysis of vonoprazan-amoxicillin first-line dual therapy on eradicating *H. pylori* based on treatment duration (A) and based on amoxicillin dose (B).

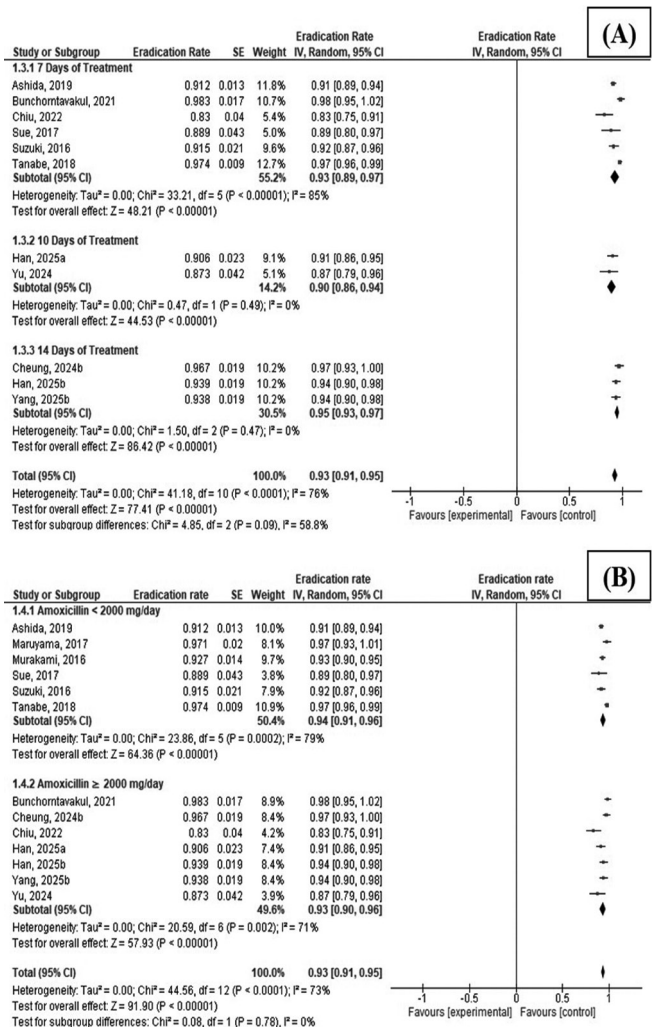

Fig. 3. Forest plot analysis of vonoprazan-amoxicillin first-line triple therapy on eradicating *H. pylori* based on treatment duration (A) and based on amoxicillin dose (B).

(1 study) had an ER of 0.99 (95%CI: 0.96-1.0) compared to 0.95 (95%CI: 0.92-0.98) in the group with a duration of therapy of 14 days as shown in Fig. 4. In the combined effect, this meta-analysis showed that the dual, triple, and quadruple therapy regimens had ERs of 0.92 (95%CI: 0.89-0.95), 0.93 (95%CI: 0.9-0.95); and 0.96 (95%CI: 0.93-0.99) respectively. Overall, VPZ-amoxicillin therapy had an ER of 0.94 (95%CI: 0.91-0.96) as shown in Supplementary file, Fig. 2.

Efficacy of VPZ-Amoxicillin Compared to PPI-based Regiment

The comparison of VPZ-amoxicillin compared to PPI-based regimens in eradicating *H. pylori* was also analyzed in this meta-analysis. Fig. 5 below shows that the RD in the ability to eradicate *H. pylori* tends to be better in the vonoprazan-amoxicillin group with an overall RD value reaching 0.06 (95%CI: 0.02–0.09; p=0.001) which indicates

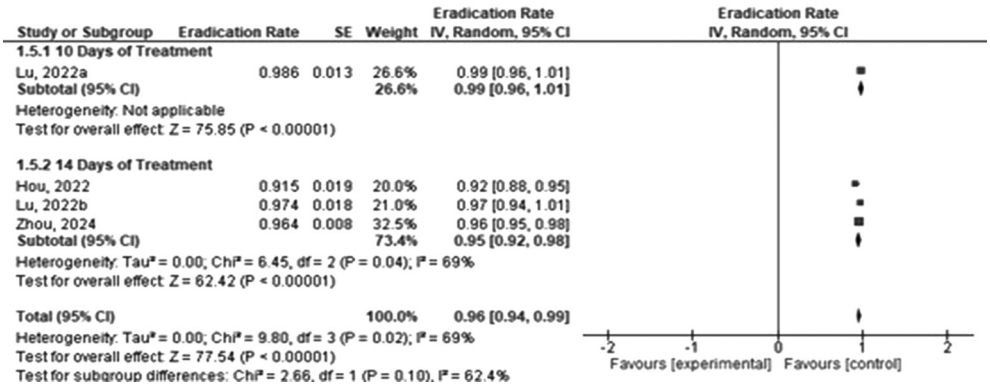

Fig. 4. Forest plot analysis of vonoprazan-amoxicillin first-line quadruple therapy on eradicating *H. pylori* based on treatment duration.

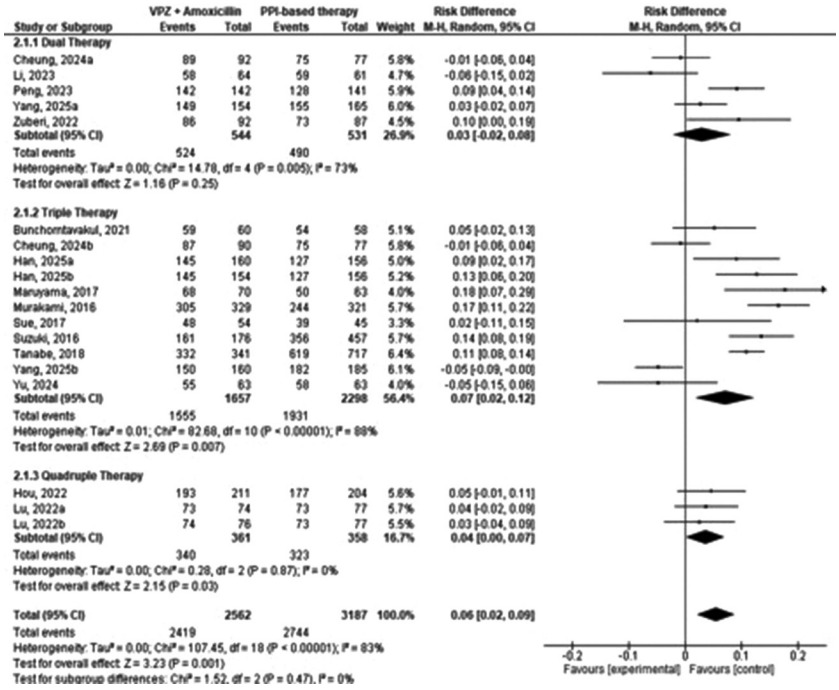

Fig. 5. Forest plot analysis of vonoprazan-amoxicillin first-line therapy on eradicating *H. pylori* compare to PPI-based therapy based on vonoprazan-amoxicillin regiment.

the superiority of VPZ in dual, triple, and quadruple therapy regimens reaching 0.03 (95%CI: -0.02–0.08), 0.07 (95%CI: 0.02 -0.12), and 0.04 (95%CI: 0–0.07). These results indicate that the comparison in the triple therapy regimen shows the highest superiority.

A meta-analysis was also conducted to evaluate the comparison of VPZ-amoxicillin to PPIs-based therapy categorized based on the dominant PPI type used in the study. The results of the data analysis showed that the comparison of VPZ-amoxicillin to omeprazole, lansoprazole, rabeprazole, and esomeprazole had a RD of 0.07 (95%CI: 0.01–0.13), 0.11 (95%CI: 0.07–0.15), 0.18 (95%CI: 0.07–0.29) (1 study) and 0.02 (95%CI: -0.01 – 0.06). These results indicate that VPZ-amoxicillin has superiority over all PPI types, especially in regimens using omeprazole and lansoprazole which showed significant results as shown in Supplementary file, Fig. 3. Comparison of additional therapy types as comparators to VPZ-amoxicillin was also conducted in this study, both comparators with PPI only and PPI with bismuth-based therapy as shown in Supplementary file, Fig 4. The results of data analysis showed that when compared with PPI only, VPZ-amoxicillin had a better eradication rate, with a risk difference of 0.09 (95%CI: 0.06-0.13). When compared with PPI + bismuth regimen, VPZ-amoxicillin showed results that were not inferior and even tended to be superior although with non-significant statistics, namely with a RD of 0.02 (95%CI: - 0.01 - 0.06).

Meta-Regression

Meta-regression was used to assess the association between covariates in numerical data and their impact on the overall test results. The meta-regression results showed that age significantly influenced the effectiveness of VPZ-amoxicillin in eradicating *H. pylori*, with a coefficient of 7.65 and a p-value of 0.006. This indicates that the older the patient, the greater the effectiveness of vonoprazan-amoxicillin. Analysis of BMI showed that BMI had no effect on the effectiveness of VPZ-amoxicillin in eradicating *H. pylori*, with a coefficient of 0.67 and a p-value of 0.411, as shown in Fig. 6 (A-B).

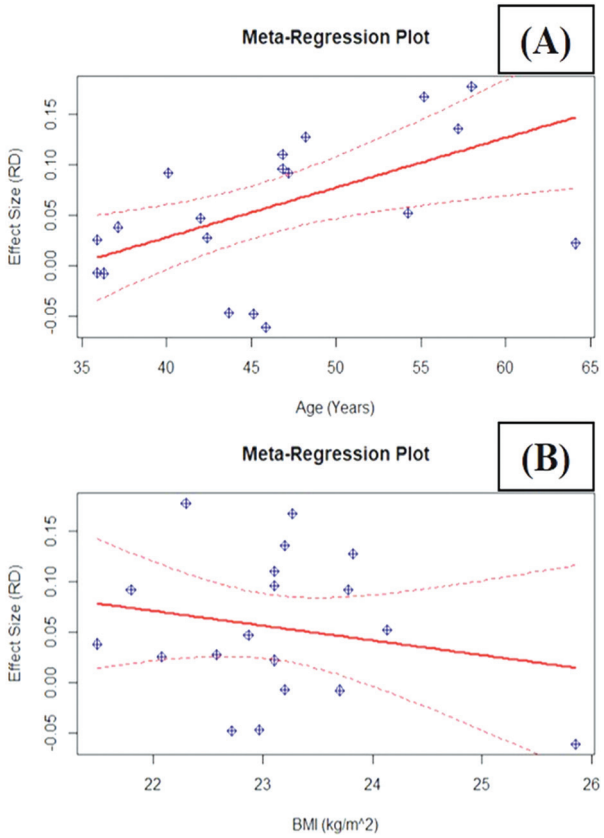

Fig. 6. Bubble plot of meta-regression. The effect of age (A) and BMI (B)as the moderator for risk different of the vonoprazan-amoxicillin therapy for eradicating *H. pylori*.

Analysis Publication Bias

Publication bias analysis was also performed in this study using Begg's funnel plot. The results of the analysis are shown in Supplementary file, Fig. 4. The results of the analysis in Supplementary file, Fig. 4 A-F show a single arm of the effectiveness of VPZ-amoxicillin alone in eradicating *H. pylori* with data distribution that tends to be centralized in the therapeutic range indicating a high ER. Supplementary file, Fig. 4 G-I shows a low potential for publication bias in comparing VPZ-amoxicillin with PPI-based therapy as explained by the symmetrical data distribution in the funnel plot.

DISCUSSION

This meta-analysis shows that the combination of VPZ and amoxicillin is highly effective in eradicating *H. pylori* in Asian populations, with an overall ER of 0.94 (95%CI: 0.91–0.96). When analyzed by treatment regimen, ERs were 0.92 (95%CI: 0.90–0.95) for dual therapy, 0.93 (95%CI: 0.91–0.95) for triple therapy, and 0.96 (95%CI: 0.93–0.99) for quadruple therapy. These values indicate that all VPZ-based regimens fall into the highly effective regimen category (>90%), indicating stability of results across populations and studies. These data align with the results of randomized clinical trials included in the analysis, including studies by Hu et al. [33], Han [16], Cheung et al [30], and several others. All these studies reported ERs above 90% for regimens using VPZ–amoxicillin, whether as dual, triple, or quadruple therapy. Specifically, Hu et al. (2025) [33] found > 90% ER with a 14-day VPZ–amoxicillin dual regimen, while Han et al. (2025) [16] showed similar results with a 95% ER and minor, insignificant side effects. A study by Cheung et al. [30] in Hong Kong also reported >90% ER with the same regimen, using a double-blind, randomized trial design and assessing outcomes using a 13C-urea breath test four weeks post-therapy.

Physiopathologically, the superiority of the VPZ-based regimen stems from its pharmacodynamic characteristics as a potassium-competitive acid blocker, which reversibly inhibits H^+/K^+-ATPase channels through competition with potassium ions [39]. This mechanism differs from proton pump inhibitors (PPIs), which require activation in an acidic environment to form a covalent bond with the active proton pump. Because it does not rely on acid activation, VPZ produces a rapid onset of action (≤1 hour), a long duration of effect (≥24 hours), and more stable acid suppression than PPIs [40, 41].

Consistent acid suppression plays a critical role in the effectiveness of *H. pylori* eradication. Antibiotics such as amoxicillin exhibit optimal bactericidal activity at near-neutral pH, due to increased stability of the beta-lactam ring and more effective mucosal penetration. By maintaining a gastric pH above 6 throughout the day, VPZ increases the antibiotic's effective exposure time to the bacteria (time above MIC), facilitating active replication of *H. pylori*, making it more susceptible to amoxicillin. Triple and quadruple regimens yield slightly higher ERs than dual regimens, reflecting the synergistic contribution of clarithromycin, metronidazole, or bismuth. Bunchorntavakul et al. [28] reported that the combination of vonoprazan, amoxicillin, and clarithromycin resulted in an eradication rate of over 93%, while the quadruple regimen achieved 96%. The addition of bismuth has pharmacological effects by inhibiting bacterial adhesion to the mucosal epithelium, disrupting biofilm formation, and enhancing antibiotic penetration into the gastric mucus layer [1, 42, 43].

Additional analysis showed that a 14-day therapy duration provided the highest ER compared to a 7- or 10-day regimen. This finding was also reported by Hu et al [25], who showed that extending the duration of therapy increased eradication from 88% to over 93% without significantly increasing side effects. Pharmacologically, this can be explained by *H. pylori*'s slow replication rate (approximately 4–6 times per day), so a longer therapy duration allows antibiotic exposure to the entire bacterial population at various growth phases. The 14-day duration also minimizes the risk of relapse due to recrudescence of bacteria that have not been fully eliminated [25].

In addition to duration, the amoxicillin dose also plays a crucial role. Analysis shows that higher doses result in better eradication rates. Pharmacodynamically, amoxicillin is time-dependent, meaning its effectiveness depends on the length of time the plasma concentration remains above the MIC. Therefore, increasing the dose not only prolongs the time above the MIC but also offsets potential fluctuations in mucosal pH that may persist even with optimal acid suppression. Studies such as Li et al. [44] and Hou et al. [25] show that high-dose amoxicillin (2.5–3 g/day) increases eradication by >94% compared to the conventional dose (2 g/day). From a drug metabolism perspective, VPZ's advantage is also evident in its stable plasma levels, which are not affected by CYP2C19 genetic polymorphisms, which are common in Asian populations. In contrast, PPIs have high interindividual variability due to their dependence on this enzymatic activity. This explains why VPZ demonstrates consistent high eradication rates across Asian countries, despite genetic variation and patient dietary patterns [45].

Comparison between the VPZ–amoxicillin regimen and PPI-based therapy showed statistically and clinically significant differences, with an overall RD of 0.06 (95%CI: 0.02–0.09). RD values for the dual, triple, and quadruple regimens were 0.03 (95%CI: –0.02 to 0.08), 0.07 (95%CI: 0.02–0.12), and 0.04 (95%CI: 0–0.07), respectively. This absolute increase of approximately 6% indicates a clear superiority of VPZ over PPIs, especially in the triple regimen. These results are consistent with empirical data from various studies. Han et al. [16] reported 91% eradication in the VPZ–amoxicillin–clarithromycin group compared to 83% in the esomeprazole-based regimen ($p<0.05$), while Cheung et al. [30] found 90% eradication in the VPZ group compared to 84% in the lansoprazole group. Additional analysis showed that VPZ's greatest superiority over lansoprazole compared to other PPIs such as omeprazole or esomeprazole. This is likely related to lansoprazole's pharmacokinetic profile, which has a shorter half-life and greater metabolic variability, leading to wider intragastric pH fluctuations and reduced antibiotic stability [30]where primary resistance rates of clarithromycin and levofloxacin are >30%. Methods: This was an investigator-initiated, three-arm, randomized clinical trial in Southern China. Between March 2022 and August 2023, treatment-naïve HP-infected adults were randomly assigned to receive one of three 14-day regimens (1:1:1 ratio.

The mechanism of VPZ's superiority can be explained physiopathologically through three main aspects. First, rapid and stable acid suppression allows the intragastric environment to reach a pH >6 within a short time, facilitating active *H. pylori* replication and increasing antibiotic efficacy. Second, it optimizes the activation of pH-dependent antibiotics such as amoxicillin and clarithromycin. Third, sustained bacteriological activity for 24 hours prevents bacterial dormancy, a major cause of PPI-based therapy failure. In the context of triple therapy, VPZ also exhibits a synergistic interaction between clarithromycin and amoxicillin. Clarithromycin inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit, while amoxicillin inhibits cell wall formation. At a stable pH, both agents act on actively proliferating bacterial populations, producing a simultaneous bactericidal effect [46, 47].

Additional analysis demonstrated that the combination of VPZ-amoxicillin was non-inferior to PPI and bismuth-based therapy. Several studies reported that the eradication efficacy of dual or triple VPZ regimens was equivalent to that of quadruple PPI and bismuth-based regimens, with eradication differences of <3% and confidence intervals crossing zero [15, 28]. This finding is important because bismuth-based regimens are often associated with poorer tolerability and higher gastrointestinal side effects [15, 28]. Thus, VPZ–amoxicillin offers comparable efficacy to complex regimens, but with a better safety and adherence profile. Furthermore, the superior pharmacodynamics of VPZ explain the stability of its effect in the context of increasing antibiotic resistance. Studies by Li et al. [44] and Hou et al. [38] showed that VPZ's efficacy remained high even in isolates with clarithromycin resistance, while PPI-based regimens showed a significant decrease. This indicates that the key factor for success is not only antibiotic selection but also pH stability, which maximizes the pharmacological activity of the antibiotic used [38, 44].

Heterogeneity analysis between studies revealed moderate variation, with the main sources being differences in age, amoxicillin dose, and duration of therapy. Meta-regression results showed that patient age (p=0.006) significantly influenced therapy effectiveness, while BMI (p = 0.411) showed no significant association. Meta-regression results showed a positive relationship between age and effect size (RD), with increasing age correlating with higher therapy effectiveness. These findings indicate that older patients demonstrate a better *H. pylori* eradication response to the VPZ-amoxicillin combination. Physiologically, this may be related to decreased basal acid secretion activity in older age, which allows for faster and longer-lasting gastric pH stability. This condition enhances the bactericidal activity of amoxicillin in a neutral environment, thereby enhancing overall eradication effectiveness [31, 32]. The absence of an effect of BMI indicates that the pharmacokinetics of VPZ and amoxicillin are relatively stable across variations in body mass, as both have a volume of distribution independent of systemic adiposity. Despite inter-study variation in duration and regimen, all results demonstrate a consistent direction of effect, with vonoprazan superior to PPIs. Therefore, the heterogeneity does not affect the validity of the main conclusions of this meta-analysis but rather reflects physiological variations and population characteristics in a real-world clinical setting [48].

Although this meta-analysis and meta-regression provides a comprehensive understanding of the effectiveness of the VPZ–amoxicillin combination, there are several limitations that need to be noted. Variations in study design, differences in amoxicillin dose, duration of therapy, and type of comparison regimen can produce residual heterogeneity that cannot be completely eliminated. In addition, some studies had incomplete data reporting, especially regarding demographic characteristics and important clinical variables, thereby limiting the power of meta-regression analyzes and increasing the potential for ecological bias because analyzes were conducted at the study level, not the individual level. Other limitations include varying methodological quality between studies, including blinding that was not always performed, which may influence the overall effect estimate.

CONCLUSIONS

The combination of VPZ and amoxicillin demonstrated high efficacy as a first-line therapy for *H. pylori* eradication in Asian populations, with success rates exceeding 90%. This therapy consistently outperformed PPI-based regimens, particularly lansoprazole, and remained comparable to PPI + bismuth regimens. 14-day duration and higher amoxicillin dose improved eradication outcomes.

Conflicts of interest: None to declare.

Authors' contribution: I.M.S.W. contributed to concept and design of the study, data acquisition, statistical analysis, data interpretation, drafting, approved the final version to be published, and agree to be accountable for all aspects of the work. I.G.E.H. contributed to the statistical analysis, data interpretation, drafting, approved the final version to be published, and agree to be accountable for all aspects of the work.

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Supplementary material: To access the supplementary material visit the online version of the *J Gastrointestin Liver Dis* at http://dx.doi.org/10.15403/jgld-6600

REFERENCES

1. Hu Y, Zhu Y, Lu N H. The management of Helicobacter pylori infection and prevention and control of gastric cancer in China. Front Cell Infect Microbiol. 2022;12:1049279. doi:10.3389/fcimb.2022.1049279
2. Ishibashi F, Suzuki S, Nagai M, Mochida K, Morishita T. Optimizing Helicobacter pylori Treatment: An Updated Review of Empirical and Susceptibility Test Based Treatments. Gut Liver. 2023;17(5):684–697. doi:10.5009/gnl220429
3. Quach DT, Vilaichone R K, Vu KV, Yamaoka Y, Sugano K, Mahachai V. Helicobacter pylori Infection and Related Gastrointestinal Diseases in Southeast Asian Countries: An Expert Opinion Survey. Asian Pac J Cancer Prev. 2018;19(12):3565–3569. doi:10.31557/APJCP.2018.19.12.3565

4. Fock KM, Ang TL. Epidemiology of Helicobacter pylori infection and gastric cancer in Asia. J Gastroenterol Hepatol. 2010;25(3):479–486. doi:10.1111/j.1440-1746.2009.06188.x
5. Aumpan N, Mahachai V, Vilaichone R K. Management of Helicobacter pylori infection. JGH Open. 2023;7(1):3–15. doi:10.1002/jgh3.12843
6. Suzuki S, Kusano C, Horii T, Ichijima R, Ikehara H. The Ideal Helicobacter pylori Treatment for the Present and the Future. Digestion. 2022;103(1):62–68. doi:10.1159/000519413
7. Argueta EA, Moss SF. Treatment of Helicobacter pylori. Curr Opin Gastroenterol. 2019;35:544–550. doi:10.1097/MOG.0000000000000578
8. Gisbert JP. Helicobacter pylori related diseases. Gastroenterol Hepatol. 2016;39(Suppl 1):36–46. doi:10.1016/S0210-5705(16)30173-X
9. Shih C A, Wu D C, Shie C B, Hsu P I. Dual Therapies Containing an Antibiotic Plus a Proton Pump Inhibitor or Vonoprazan for Helicobacter pylori Infection: A Systematic Review. Microorganisms. 2025;13(4):715. doi:10.3390/microorganisms13040715
10. Echizen H. The First in Class Potassium Competitive Acid Blocker, Vonoprazan Fumarate: Pharmacokinetic and Pharmacodynamic Considerations. Clin Pharmacokinet. 2016;55(4):409–418. doi:10.1007/s40262-015-0326-7
11. Abadi ATB, Ierardi E. Vonoprazan and Helicobacter pylori Treatment: A Lesson From Japan or a Limited Geographic Phenomenon? Front Pharmacol. 2019;10:316. doi:10.3389/fphar.2019.00316
12. Ju KP, Kong QZ, Li YY, Li YQ. Low dose or high dose amoxicillin in vonoprazan based dual therapy for Helicobacter pylori eradication? A systematic review and meta analysis. Helicobacter. 2024;29:e13054. doi:10.1111/hel.13054
13. Shirley M. Vonoprazan: A Review in Helicobacter pylori Infection. Drugs. 2024;84:319–327. doi:10.1007/s40265-024-01943-4
14. Liu L, Nahata MC. Vonoprazan With Amoxicillin or Amoxicillin and Clarithromycin for the Treatment of Helicobacter pylori Infection. Ann Pharmacother. 2023;57:1185–1197. doi:10.1177/10600280231170413
15. Hu Y, Xu X, Liu XS, He C, Ouyang YB, Li NS, et al. Fourteen day vonoprazan and low or high dose amoxicillin dual therapy for eradicating Helicobacter pylori infection: A prospective, open label, randomized non inferiority clinical study. Front Immunol. 2023;13:1086513. doi:10.3389/fimmu.2022.1086513
16. Han RS, Hao JW, Wang T, Xin Z, Fan GX, Wang GD, et al. Efficacy and safety of triple therapy with vonoprazan for Helicobacter pylori eradication: A multicenter, prospective, randomized controlled trial. World J Gastroenterol. 2025;31:1–13. doi:10.3748/wjg.v31.i1.1
17. Graham DY, Lu H, Shiotani A. Vonoprazan containing Helicobacter pylori triple therapies: contribution to global antimicrobial resistance. J Gastroenterol Hepatol. 2021;36:1159–1163. doi:10.1111/jgh.15387
18. Graham DY. Why the vonoprazan Helicobacter pylori therapies in the US European trial produced unacceptable cure rates. Dig Dis Sci. 2023;68:1691–1697. doi:10.1007/s10620-023-07886-5
19. Ashida K, Honda Y, Sanada K, Takemura Y, Sakamoto S. The safety and effectiveness of vonoprazan based Helicobacter pylori eradication therapy: a prospective post marketing surveillance. Expert Opin Drug Saf. 2019;18:1255–1261. doi:10.1080/14740338.2019.1676722
20. Li J, Lv L, Zhu Y, Zhou Z, He S. A Modified 14 Day Dual Therapy with Vonoprazan and Amoxicillin Amplified the Advantages Over Conventional Therapies for Eradication of Helicobacter pylori: A Non Inferiority Clinical Trial. Infect Drug Resist. 2023;16:5637–5645. doi:10.2147/IDR.S417711
21. Murakami K, Sakurai Y, Shiino M, Funao N, Nishimura A, Asaka M. Vonoprazan, a novel potassium competitive acid blocker, as a component of first line and second line triple therapy for Helicobacter pylori eradication: a phase III, randomised, double blind study. Gut. 2016;65(9):1439–1446. doi:10.1136/gutjnl-2015-311304
22. Tanabe H, Yoshino K, Ando K, Nomura Y, Ohta K, Satoh K, et al. Vonoprazan based triple therapy is non inferior to susceptibility guided proton pump inhibitor based triple therapy for Helicobacter pylori eradication. Ann Clin Microbiol Antimicrob. 2018;17:29. doi:10.1186/s12941-018-0281-x
23. Li Y, Chang N, Han X, Liang D, Jiang S, Li K K. Comparison of vonoprazan with different frequency amoxicillin regimens in the treatment of Helicobacter pylori infections: A retrospective study. Medicine (Baltimore). 2025;104:e43998. doi:10.1097/MD.0000000000043998
24. Yang X E, Zhang S J, Liu Y, Yao S Y, Zhang S X, Liu X M, et al. Amoxicillin high dose dual therapy for Helicobacter pylori primary eradication: Proton pump inhibitor and potassium competitive acid blocker, which's better? World J Gastroenterol. 2025;31:100863. doi:10.3748/wjg.v31.i13.100863
25. Hu Y, Xu X, Ouyang Y B, He C, Li N S, Xie C, et al. Optimization of vonoprazan amoxicillin dual therapy for eradicating Helicobacter pylori infection in China: A prospective, randomized clinical pilot study. Helicobacter. 2022;27:e12896. doi:10.1111/hel.12896
26. Zhou J, Jia L, Liu Z, Zhao W, Liu L, Chen X, et al. Efficacy and safety of vonoprazan based bismuth quadruple therapy for first line Helicobacter pylori eradication: A large scale, real world study. Medicine (Baltimore). 2024;103:e40170. doi:10.1097/MD.0000000000040170
27. Suzuki S, Gotoda T, Kusano C, Iwatsuka K, Moriyama M. The efficacy and tolerability of a triple therapy containing a potassium competitive acid blocker compared with a 7 day PPI based low dose clarithromycin triple therapy. Am J Gastroenterol. 2016;111:949–956. doi:10.1038/ajg.2016.182
28. Bunchorntavakul C, Buranathawornsom A. Randomized clinical trial: 7 day vonoprazan based versus 14 day omeprazole based triple therapy for Helicobacter pylori. J Gastroenterol Hepatol. 2021;36:3308–3313. doi:10.1111/jgh.15700
29. Chiu YT, Lee FJ, Kuo CY, Lin YC, Liang KS, Tseng LW, et al. Seven day vonoprazan based triple therapy as first line Helicobacter pylori treatment in comparison with extended sequential therapy. JGH Open. 2023;7:105–109. doi:10.1111/hel.13129
30. Cheung KS, Lyu T, Deng Z, Han S, Ni L, Wu J, et al. Vonoprazan dual or triple therapy versus bismuth quadruple therapy as first line therapy for Helicobacter pylori infection: A three arm, randomized clinical trial. Helicobacter. 2024;29:e13040. doi:10.1111/hel.13133
31. Lu L, Wang Y, Ye J, Han Y, Lou G, Li Y, et al. Quadruple therapy with vonoprazan 20 mg daily as a first line treatment for Helicobacter pylori infection: A single center, open label, noninferiority, randomized controlled trial. Helicobacter. 2023;28:e12941. doi:10.1111/hel.12940
32. Maruyama M, Tanaka N, Kubota D, Miyajima M, Kimura T, Tokutake K, et al. Vonoprazan based regimen is more useful than PPI based one as a first line Helicobacter pylori eradication: A randomized controlled trial. Can J Gastroenterol Hepatol. 2017;2017:4385161. doi:10.1155/2017/4385161
33. Hu Y, Zhang ZY, Wang F, Zhuang K, Xu X, Liu DS, et al. Effects of amoxicillin dosage on cure rate, gut microbiota, and antibiotic resistome in vonoprazan and amoxicillin dual therapy for Helicobacter pylori: A multicentre, open label, non inferiority randomized controlled trial. Lancet Microbe. 2025;6:1–11. doi:10.1016/j.lanmic.2024.100975
34. Yu J, Cui C, Ma K, Yang P, Jiang Y, Wang X. Effectiveness and safety of vonoprazan and amoxicillin dual regimen with Saccharomyces boulardii supplements on eradication of Helicobacter pylori. BMC Gastroenterol. 2024;24:123. doi: 10.1186/s12876-024-03524-0

35. Zuberi BF, Ali FS, Rasheed T, Bader N, Hussain SM, Saleem A. Comparison of vonoprazan and amoxicillin dual therapy with standard triple therapy with proton pump inhibitor for Helicobacter pylori eradication: A randomized control trial. Pak J Med Sci. 2022;38:965–969. doi:10.12669/pjms.38.4.5436
36. Sue S, Ogushi M, Arima I, Kuwashima H, Nakao S, Naito M, et al. Vonoprazan vs proton pump inhibitor based first line 7 day triple therapy for clarithromycin susceptible Helicobacter pylori: A multicenter, prospective, randomized trial. Helicobacter. 2018;23:e12466. doi:10.1111/hel.12456
37. Peng X, Chen HW, Wan Y, Su PZ, Yu J, Liu JJ, et al. Combination of vonoprazan and amoxicillin as the first line Helicobacter pylori eradication therapy: A multicenter, prospective, randomized, parallel controlled study. Clin Exp Med. 2023;23:4011–4019. doi:10.1007/s10238-023-01074-5
38. Hou X, Meng F, Wang J, Sha W, Chiu CT, Chung WC, et al. Vonoprazan non inferior to lansoprazole in treating duodenal ulcer and eradicating Helicobacter pylori in Asian patients. J Gastroenterol Hepatol. 2022;37:1275–1283. doi:10.1111/jgh.15837
39. Remitha NPSI, Dewi NPRP, Kusuma KWA, Sasmana IGAP, Supadmanaba IGP, Sindhughosa DA, et al. Efficacy and safety of lenvatinib versus atezolizumab plus bevacizumab in the treatment of unresectable hepatocellular carcinoma: A systematic review and meta analysis. Asian Pac J Cancer Prev. 2025;26:1529–1542. doi:10.31557/APJCP.2025.26.5.1529
40. Sun Y, Yue L, Hu W. Effectiveness and safety of vonoprazan based regimens compared with proton pump inhibitor based regimens as first line agents for Helicobacter pylori: A meta analysis of randomized clinical trials. Eur J Clin Pharmacol. 2023;79:279–288. doi:10.1007/s00228-022-03430-y
41. Al Fakhrany OM, Elekhnawy E. Helicobacter pylori in the post antibiotics era: from virulence factors to new drug targets and therapeutic agents. Arch Microbiol. 2023;205:301. doi:10.1007/s00203-023-03639-0
42. Furuta T, Yamade M, Higuchi T, Takahashi S, Ishida N, Tani S, et al. Expectations for the dual therapy with vonoprazan and amoxicillin for the eradication of H. pylori. J Clin Med. 2023;12:253. doi:10.3390/jcm12093110
43. Sugimoto M, Yamaoka Y. Role of vonoprazan in Helicobacter pylori eradication therapy in Japan. Front Pharmacol. 2018;9:1560. doi:10.3389/fphar.2018.01560
44. Li J, Lv L, Zhu Y, Zhou Z, He S. A modified 14 day dual therapy with vonoprazan and amoxicillin amplified the advantages over conventional therapies for eradication of Helicobacter pylori: A non inferiority clinical trial. Infect Drug Resist. 2023;16:5637–5645. doi:10.2147/IDR.S417711
45. Kagami T, Sahara S, Ichikawa H, Uotani T, Yamade M, Sugimoto M, et al. Potent acid inhibition by vonoprazan in comparison with esomeprazole, with reference to CYP2C19 genotype. Aliment Pharmacol Ther. 2016;43:1048–1059. doi:10.1111/apt.13588
46. Grosso R, de Paz M V. Scope and limitations of current antibiotic therapies against Helicobacter pylori: reviewing amoxicillin gastroretentive formulations. Pharmaceutics. 2022;14:2103. doi:10.3390/pharmaceutics14071340
47. Zhou B G, Jiang X, Ding Y B, She Q, Li Y Y. Vonoprazan–amoxicillin dual therapy versus bismuth containing quadruple therapy for Helicobacter pylori eradication: A systematic review and meta analysis. Helicobacter. 2024;29:e13040. doi:10.1111/hel.13040
48. Zhang WL, Lin BS, Li YY, Ding YM, Han ZX, Ji R. Efficacy and safety of vonoprazan and amoxicillin dual therapy for Helicobacter pylori eradication: A systematic review and metaanalysis. Digestion. 2023;104:249–261. doi:10.1159/000529622