Zifam Novocid

Vonoprazan Tablets 10/20 mg

MONOGRAPH

Contents

INTRODUCTION

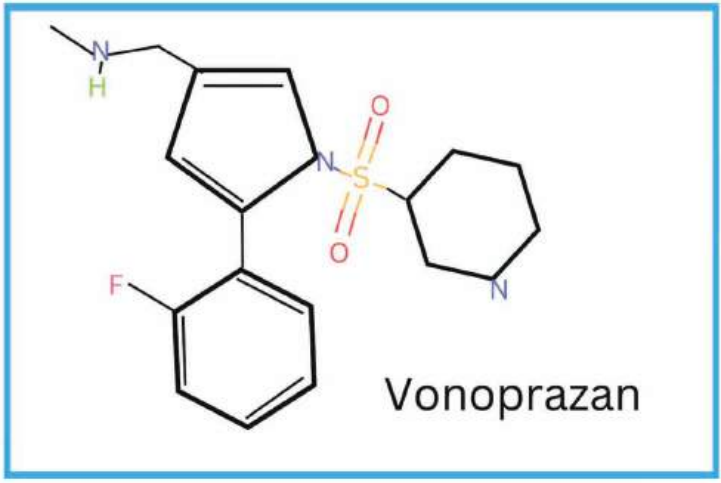
The preferred treatment for many gastric diseases, especially gastric acid-related diseases, has been the proton pump inhibitor (PPI). Such gastric acid-related conditions are not limited to symptomatic gastroesophageal reflux disease (GERD), erosive esophagitis, dyspepsia, chronic gastritis, gastric and duodenal ulcers, and Helicobacter pylori infection. However, despite being an effective acid suppression and only 1-3% of short-term adverse events, a recent umbrella review indicated more longer-term risks with PPI use, especially fractures and kidney disease in the elderly, and a more severe COVID-19 disease. Furthermore, an estimated 10-40% of GERD patients have an incomplete or no response to standard doses of PPI, otherwise termed refractory GERD. Thus, the aforementioned limitations warrant an alternative acid-suppressive drug superior to or at least similar in efficacy to PPI.

Recently, a novel potassium-competitive acid blocking (PCAB) agent called vonoprazan, has been developed that is stronger, faster, and exhibits longer-lasting acid suppression than conventional PPIs. The acid-inhibitory effect of vonoprazan has been reported to be more potent than that of PPIs, with greater impact against acid-related diseases such as GERD, Helicobacter pylori infection, gastric and duodenal ulcers, and prevention of recurrence in nonsteroidal anti-inflammatorydrug or low-dose-aspirin ulcer.

PRODUCT INFORMATION

Description

Vonoprazan is an oral potassium-competitive acid blockers (PCAB) used for the treatment of Gastric ulcer and Duodenal ulcer, Reflux esophagitis, Prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration, Prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) administration, Adjunct to Helicobacter pylori eradication.

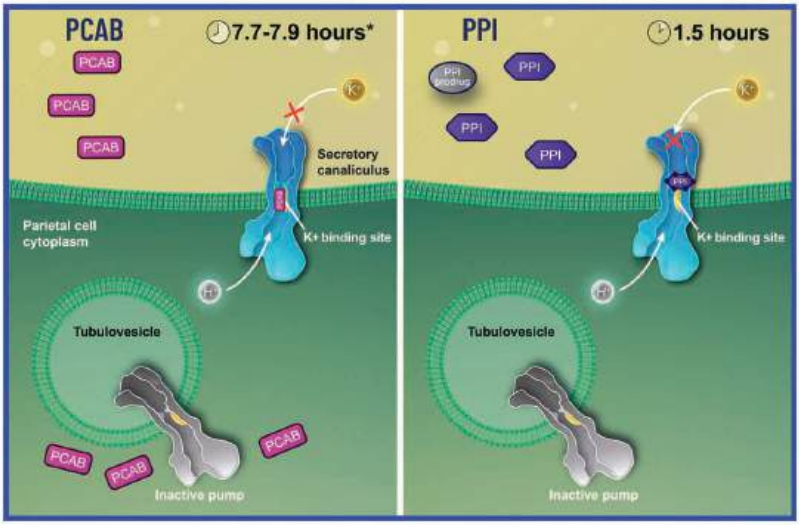


CLINICAL PHARMACOLOGY

Mechanism of Action

Vonoprazan is a potassium competitive acid blocker (P-CAB) and does not require activation by acid. It inhibits H+, K+-ATPase in a reversible and potassium-competitive manner. Vonoprazan has a strong basicity and resides on the acid production site of gastric parietal cells for a long time, thereby inhibiting gastric acid production.

Vonoprazan exerts a strong inhibitory effect on formation of mucosal damage in upper part of the gastrointestinal tract. The role of Vonoprazan in the Helicobacter pylori eradication is considered to increase intragastric pH leading to the enhancement of antibacterial activity of amoxicillin, clarithromycin and metronidazole which are concomitantly administered.



Differentiated Mechanism of Action Between PCABs and PPIs (Laine, et al., 2022)

	PPIs	PCABs
Symptom Control	Full effect after 3-5 days	Full effect after the 1st dose
Plasma half-life	2 hours	7-9 hours
Influence of meal	Before Meal	With or without meal
Type of drug	Prodrug (Enteric coated)	Active form
Acidic Medium	Required	Not required
Type of Inhibition	Irreversible	Reversible

Pharmacokinetics and Pharmacodynamics

Pharmacokinetics at consecutive administration of a daily dose of 10mg or 20mg of Vonoprazan in healthy adult male subjects once daily for 7 days, AUC (0-tau) and Cmax increase as the dose increases.

The degree of these increases is slightly higher than the dose ratio. It is considered that the steady state has been reached by day 3 of administration, since the trough level of the blood concentration of Vonoprazan is constant between day 3 and day 7 of administration. In addition, it is considered that pharmacokinetics of Vonoprazan at consecutive administration may not be time-dependent, as the result of the evaluation of accumulation with regard to AUC (0-tau) and T1/2 of Vonoprazan.

Dose Condition	10mg	20mg
Tmax (h)	1.5 (0.75, 3.0)	1.5 (0.75, 3.0)
Cmax (ng/ml)	12.0 ± 1.8	26.3± 6.6
T1/2 (h)	7.0 ± 1.6	6.1 ± 1.2
AUC(0-tau) (ng.h/ml)	79.5 ± 16.1	151.6 ± 40.3
Mean ± S.D. of 9 subjects | [Tmax is expressed by the median (minimum value, maximum value)]		

Distribution

The protein binding rate is 85.2 to 88.0% when Vonoprazan in the range of 0.1 to 10ug/mL is added to human plasma (in vitro).

Metabolism

Vonoprazan is metabolized mainly by hepatic drug-metabolizing enzyme CYP3A4 and partially by CYP2B6, CYP2C19 and CYP2D6. Vonoprazan is also metabolized by sulfo-transferase SULT2A1 (in vitro).

Vonoprazan exhibits time-dependent inhibitory effect on CYP2B6, CYP2C19 and CYP3A4/5 (in vitro).

In addition, Vonoprazan shows a slight concentration-dependent inductive effect on CYP1A2 but it shows little inductive effect on CYP2B6 and CYP3A4/5 (in vitro).

Elimination

When radioactive-labelled drug (as Vonoprazan) is orally administered to healthy adult male subjects, 98.5% of the radioactivity administered is excreted into urine and feces by 168 hours after administration: 67.4% into urine and 31.1% into feces.

DOSAGE AND ADMINISTRATION

Gastric ulcer and duodenal ulcer

The usual adult dosage for oral use is 20mg of Vonoprazan administered orally once daily an 8 weeks treatment for gastric ulcer and a 6 weeks treatment for duodenal ulcer.

Reflux esophagitis

The usual adult dose for oral use is 20mg of Vonoprazan administered once daily for a total of 4 weeks of treatment. If that dosing proves insufficient, the administration should be extended, but for no longer than 8 weeks of treatment.

For the maintenance therapy of reflux esophagitis showing recurrence and recrudescence, the dose for oral use is 10mg of Vonoprazan once daily.However, when the efficacy is inadequate, the dosage may be increased up to 20mg of Vonoprazan once daily.

Prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration

The usual adult dosage is one tablet of 10mg of Vonoprazan administered orally once daily.

Prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) administration.

The usual adult dosage is one tablet of 10mg of Vonoprazan administered orally once daily.

Adjunct to Helicobacter pylori eradication

For adults, the following three-drug regimen should be administered orally at the same time twice daily for seven days: 20mg of Vonoprazan, 750mg of amoxicillin and 200mg of clarithromycin. The dose of clarithromycin may be increased as clinically warranted. However, dosage should not exceed 400mg twice daily.

If Helicobacter pylori eradication with a three-drug regimen comprising a proton pump inhibitor, amoxicillin and clarithromycin has been unsuccessful, as an alternative treatment, adults should be administered the following three drugs orally twice daily for seven days: 20mg of Vonoprazan, 750mg of amoxicillin and 250mg of metronidazole.

CONTRAINDICATIONS

Vonoprazan is contraindicated in:

- Patients with hypersensitivity to Vonoprazan or to any excipient of the product.
- Patients receiving atazanavir sulphate.

WARNINGS AND PRECAUTIONS

General

At the treatment the course of the disease should closely be observed and the minimum therapeutic necessity should be used according to the disease condition. In the long-term treatment with Vonoprazan, close observation by such means as endoscopy should be made.

In the maintenance of healing of reflux esophagitis, Vonoprazan should be administered only to the patients who repeat recurrence and recrudescence of the condition.Administration to the patients who do not necessitate maintenance of healing should be avoided.

When the healing is maintained over a long period and when there is no risk of recurrence, the dose reduction to a dose of 10mg from a dose 20mg, or suspension of administration should be considered.

Impaired Renal Function

Vonoprazan should be administered with care in patients with renal disorders as a delay in the excretion of Vonoprazan may occur, which may result in an increase in the concentration of Vonoprazan in the blood.

Impaired Hepatic Function

Vonoprazan should be administered with care in patients with hepatic disorders as a delay in the metabolism and excretion of Vonoprazan may occur, which may result in an increase in the concentration of Vonoprazan in the blood.

Clostridium difficile, serious colitis, including pseudo-membranous colitis

There is an increased risk of gastrointestinal infection caused by Clostridium difficile. Serious colitis accompanied with bloody stools, such as pseudomembranous colitis, may occur due to amoxicillin hydrate or clarithromycin being used for Helicobacter pylori eradication, in combination with Vonoprazan.

If abdominal pain and frequent diarrhea occur, appropriate measures, such as immediate discontinuation of the treatment, should be taken.

USES IN SPECIAL POPULATION

Use in elderly

Since the physiological functions such as hepatic or renal function are decreased in elderly patients in general, Vonoprazan should be carefully administered.

Use in children less than 18 years of age

Vonoprazan has not been studied in patients under 18 years of age.

Pregnancy

Vonoprazan should be used in pregnant women or women having possibilities of being pregnant only if the expected therapeutic benefit is thought to outweigh any possible risk.

Nursing Mothers

It is advisable to avoid the administration of Vonoprazan to nursing mothers. However, when the administration is indispensable, nursing should be discontinued.

OVERDOSE

There is no experience of overdose with Vonoprazan. Vonoprazan is not removed from the circulation by hemodialysis. If overdose occurs, treatment should be symptomatic and supportive.

ADVERSE REACTIONS

Following adverse reactions have been reported with the use of Vonoprazan: diarrhea, constipation, drug hypersensitivity (including anaphylactic shock), drug eruption, urticaria, hepatotoxicity, jaundice, rash, nausea, abdominal distension, gamma-glutamyl transferase increased, AST increased, Liver function test abnormal, ALT increased, ALP increased, LDH increased, GPT increased, edema and eosinophilia.

DRUG INTERACTIONS

Vonoprazan should be administered with care when co-administered with the following drugs:

Drugs	Signs	Mechanism & Risk Factors
CYP3A4 inhibitors Clarithromycin etc.	Blood conc. of Vonoprazan may increase	It has been reported that blood conc. of Vonoprazan increased in concomitant use with clarithromycin
Digoxin, Methyldigoxin	Effect of these drugs may be enhanced	Gastric antisecretory effect of Vonoprazan may inhibit hydrolysis of digoxin, resulting in increase in the blood concentration of digoxin
Itraconazole, Tyrosine kinase inhibitors Gefitinib, Nilotinib, Erlotinib	Effect of these drugs may be diminished	Gastric antisecretory effect of Vonoprazan may lead to a decrease in the blood concentration of these drugs

CLINICAL TRIALS

Comparison of vonoprazan and proton pump inhibitors for eradication of Helicobacter pylori

Satoshi Shinozaki a, Hiroaki Nomoto b, Yoshie Kondo b, Hirotsugu Sakamoto c, Yoshikazu Hayashi c, Hironori Yamamoto c, Alan Kawarai Lefor d, Hiroyuki Osawa c,

Kaohsiung Journal of Medical Sciences (2016) 32, 255e260

Abstract: Alternative eradication therapies for Helicobacter pylori infection are needed because of an increasing failure rate over the past decade.

Aim: This study was to determine if vonoprazan, a new potassium-competitive acid blocker, showed superiority to existing proton pump inhibitors for primary eradication of H. pylori in routine clinical practice.

Design: Data for 573 patients who underwent primary H. pylori eradication therapy were retrospectively reviewed. Regimens included clarithromycin 200 mg, amoxicillin 750 mg, and an acid suppressing drug [lansoprazole 30 mg (LAC), rabeprazole 10 mg (RAC), esomeprazole 20 mg (EAC), or vonoprazan 20 mg (VAC)] twice daily for 1 week. Eradication was successful in 73% (419/573) of patients using intention-to-treat (ITT) analysis and 76% (419/549) of patients in per-protocol (PP) analysis.

Results: The VAC group had a significantly superior eradication rate compared with the LAC and RAC groups in ITT (VAC 83%, LAC 66% and RAC 67%, $p < 0.01$) and PP analysis (VAC 85%, LAC 69% and RAC 70%, $p < 0.01$), and had a similarly high eradication rate to the EAC group (83% in ITT and 87% in PP).Although the eradication rate in the VAC and EAC groups was not significantly higher than in the LAC and RAC groups in patients with mild gastric atrophy with both ITT and PP analyses, it was significantly higher in patients with severe gastric atrophy ($p < 0.01$).

Conclusion: The VAC group had a significantly higher H. pylori eradication rate than the LAC and RAC groups, and a > 80% eradication rate regardless of the degree of atrophy. (Shinozaki, et al., 2016)

Real-world outcomes associated with vonoprazan-based versus proton pump inhibitor-based therapy for Helicobacter pylori infection in Japan

Colin W Howden[1], Erin E Cook[2], Elyse Swallow[2], Karen Yang[3], Helen Guo[4], Corey Pelletier[5], Rinu Jacob[5], Kentaro Sugano[6]

Ther Adv Gastroenterol 2023, Vol. 16: 1–12

Abstract

Background: Japanese guidelines recommend triple therapy with vonoprazan or a proton pump inhibitor (PPI) in combination with antibiotics to treat Helicobacter pylori (H. pylori) infection. While studies have shown improved eradication rates and reduced costs with vonoprazan versus PPIs, there is little data describing healthcare resource use (HCRU) and treatment patterns.

Objectives: To compare patients treated with a vonoprazan-based or PPI-based regimen for H. pylori infection in Japan in terms of their characteristics, HCRU, healthcare costs, clinical outcomes, and treatment patterns.

Design: Retrospective matched cohort.

Methods: We used data from the Japan Medical Data Center claims database (July 2014-January 2020) to identify adult patients with H. pylori infection and a first observed use of vonoprazan or a PPI in 2015 or later. Patients prescribed a vonoprazan-based or a PPI-based regimen were matched 1:1 using propensity score matching. HCRU, healthcare costs, diagnostic tests, a proxy for H. pylori eradication (i.e. no triple therapy with amoxicillin in combination with metronidazole or clarithromycin >30 days after the index date), and second-line treatment were described during the 12-month follow-up period.

Results: Among 25,389 matched pairs, vonoprazan-treated patients had fewer all-cause and H. pylori-related inpatient stays and outpatient visits than PPI-treated patients, resulting in lower all-cause healthcare costs [185,378 Japanese yen (JPY) versus 230,876 JPY, $p < 0.001$]. Over 80% of patients received a post-treatment test for H. pylori. Fewer vonoprazan-treated than PPI-treated patients subsequently received an additional triple regimen for H. pylori infection (7.1% versus 20.0%, $p < 0.001$) or a prescription for vonoprazan or a PPI as monotherapy (12.4% versus 26.4%, $p < 0.001$) between 31 days and 12 months after the index date.

Conclusion: Patients with H. pylori infection who were treated with vonoprazan-based therapy had lower rates of subsequent H. pylori treatment, lower overall and H. pylori-related HCRU, and lower healthcare costs than patients treated with PPI-based therapy. (Howden, et al., 2023)

Meta-analysis of Helicobacter pylori eradication therapy using vonoprazan as an acid suppressor compared with bismuth quadruple therapy

Hui Yang1,2 | Miao Zhang1 | Gang Ma1 | Jiaqi Yang1 | Kemei Wang1 |Shuangshuang Jiang1 | Jiaqiang Dong1 | Ying Han1

Helicobacter. 2024;29:e13059, https://doi.org/10.1111/hel.13059

Abstract

Background: Vonoprazan, a novel acid suppressant, has recently emerged as a regimen for eradicating Helicobacter pylori. However, uncertainties exist about the effectiveness and safety of VPZ-based regimens compared with those of bismuth-based quadruple therapy in eradicating H. pylori. The present meta-analysis was performed to compare the effectiveness and safety of vonoprazan-based regimens with those of bismuth quadruple therapy in eradicating H. pylori.

Materials and Methods: All randomized controlled trials and non-randomized controlled trials comparing the vonoprazan-based therapy with the bismuth quadruple therapy were included in this meta-analysis. Information was also extracted by two evaluators, and if heterogeneity existed, a random-effects model was used to calculate the combined relative ratio and 95% confidence interval; otherwise, a fixed-effects model was used. And subgroup analyses were performed to explore the sources of heterogeneity.

Results: A total of 10 studies, comprising 2587 patients were included in the meta-analysis. The results showed that the combined eradication rate of patients treated with the vonoprazan-based regimen was significantly higher than that of patients treated with bismuth quadruple therapy, in both intention-to- treat and per-protocol analyses, and the differences were statistically significant. Among the intention-to- treat analyses results: (90.28% vs. 83.64% [odds ratio (OR) = 1.85, 95% confidence interval (CI) (1.27, 2.70), p = 0.001]); in the per-protocol analyses: (94.80% vs. 89.88%, [OR = 2.25, 95% CI (1.37, 3.69), p = 0.001]). The occurrence of adverse events was significantly lower in patients treated with vonoprazan-based regimens than in those treated with bismuth quadruple therapy, (14.50% vs. 25.89%, [OR = 0.49, 95% CI (0.32, 0.75), p = 0.001]).

Conclusion: For eradicating H. pylori, vonoprazan-based regimens are remarkably advantageous over bismuth quadruple therapy. Furthermore, vonoprazan-based regimens exhibit a lower rate of adverse events than bismuth quadruple therapy. (Yang, et al., 2024)

Vonoprazan Triple and Dual Therapy for Helicobacter pylori Infection in the United States and Europe: Randomized Clinical Trial

William D. Chey, Francis Mégraud, Loren Laine, Luis J. López, Barbara J. Hunt, and Colin W. Howden1

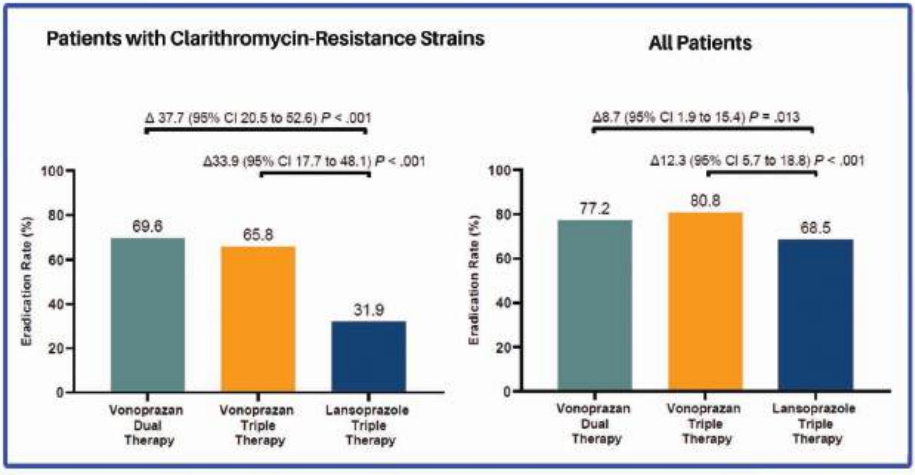
Gastroenterology 2022; 163:608-619

Background & AIMS: Novel, effective treatments for Helicobacter pylori infection are needed. This study evaluated the efficacy of vonoprazan, a potassium-competitive acid blocker, vs standard treatment on H pylori eradication in the United States and Europe.

Methods: In a randomized, controlled, phase 3 trial, treatment-naïve adults with H pylori infection were randomized 1:1:1 to open-label vonoprazan dual therapy (20 mg vonoprazan twice daily; 1 g amoxicillin 3 times daily), or double-blind triple therapy twice a day (vonoprazan 20 mg or lansoprazole 30 mg; amoxicillin 1 g; clarithromycin 500 mg) for 14 days. The primary outcome was noninferiority in eradication rates in patients without clarithromycin- and amoxicillin-resistant strains (noninferiority margin ¼ 10%). Secondary outcomes assessed superiority in eradication rates in clarithromycin-resistant infections, and in all patients.

Results: A total of 1046 patients were randomized. Primary outcome eradication rates (nonresistant strains): vonoprazan triple therapy 84.7%, dual therapy 78.5%, vs lansoprazole triple therapy 78.8% (both noninferior; difference 5.9%; 95% confidence interval [CI], 0.8 to 12.6; P < .001; difference -0.3%; 95% CI, 7.4 to 6.8; P ¼ .007, respectively). Eradication rates in clarithromycin-resistant infections: vonoprazan triple therapy 65.8%, dual therapy 69.6%, vs lansoprazole triple therapy 31.9% (both superior; difference 33.9%; 95% CI, 17.7–48.1; P < .001; difference 37.7%; 95% CI, 20.5–52.6; P < .001, respectively). In all patients, vonoprazan triple and dual therapy were superior to lansoprazole triple therapy (80.8% and 77.2%, respectively, vs 68.5%, difference 12.3%; 95% CI, 5.7–18.8; P < .001; difference 8.7%; 95% CI, 1.9–15.4; P ¼ .013). Overall frequency of treatment-emergent adverse events was similar between vonoprazan and lansoprazole regimens (P > .05).

Conclusion: Both vonoprazan-based regimens were superior to proton pump inhibitor–based triple therapy in clarithromycin-resistant strains and in the overall study population. (Chey, et al., 2022)



A comparison of efficacy and safety of potassium-competitive acid blocker and proton pump inhibitor in gastric acid-related diseases: A systematic review and meta-analysis

Daniel Martin Simadibrata, Ari Fahrial Syam and Yeong Yeh Lee

Journal of Gastroenterology and Hepatology 37 (2022) 2217–2228

Abstract

Background & Aim: Potassium-competitive acid blocker (PCAB) is a recent alternative to proton pump inhibitor (PPI) for potent acid suppression. The current systematic review and meta-analysis aimed to compare the efficacy and safety of PCAB versus PPI in treating gastric acid-related diseases.

Methods: We searched up to June 5, 2022, for randomized controlled trials of gastric acid-related diseases that included erosive esophagitis, symptomatic gastroesophageal reflux disease (GERD), peptic ulcers, and Helicobacter pylori infection. The pooled risk ratio (RR) was evaluated for the efficacy outcome and treatment-emergent adverse events (TEAEs) as the safety outcome. Sensitivity analyses were performed to test the robustness of the study findings.

Results: Of the 710 screened studies, 19 studies including 7023 participants were analyzed. The RRs for the healing of erosive esophagitis with Vonoprazan versus PPI were 1.09 (95% confidence interval [CI] 1.03–1.14), 1.03 (95% CI 1.00–1.07), and 1.02 (95% CI 1.00–1.05) in Weeks 2, 4, and 8, respectively. There were no differences in the improvement of GERD symptoms and healing of gastric and duodenal ulcers between PCAB and PPI. The pooled eradication rates of H. pylori were significantly higher in Vonoprazan versus PPI first-line treatment (RR 1.13; 95% CI 1.04–1.22). The overall RR of TEAEs with Vonoprazan versus PPI was 1.08 (95% CI 0.89–1.31). Overall, the risk of bias was low to some concerns. Furthermore, sensitivity analyses confirmed the robustness of the study's conclusion.

Conclusion: Vonoprazan is superior to PPI in first-line H. pylori eradication and erosive esophagitis but non-inferior in other gastric acid-related diseases. Likewise, short-term safety is comparable in both treatment groups. (Simadibrata, et al., 2022)

Systematic review with network meta-analysis: indirect comparison of the efficacy of vonoprazan and proton-pump inhibitors for maintenance treatment of gastroesophageal reflux disease

Hiroto Miwa, Ataru Igarashi, Lida Teng, Akihito Uda, Hisato Deguchi, Toshiro Tango
J Gastroenterol (2019) 54:718–729https://doi.org/10.1007/s00535-019-01572-y

Abstract

Background: Long-term maintenance treatment of gastro-esophageal reflux disease (GERD) is important to prevent relapse. Proton-pump inhibitors (PPIs) are used for both treatment and maintenance therapy of GERD. Recently, a potassium-competitive acid blocker vonoprazan was launched in Japan. We evaluated the comparative efficacy of vonoprazan and other PPIs for GERD maintenance.

Methods: A systematic literature search was performed using MEDLINE and Cochrane Central Register of Controlled Trials. Double-blind randomized controlled trials (RCTs) of PPIs, vonoprazan, and placebo for GERD maintenance published in English or Japanese were selected. Among them, studies conducted at the recommended dose and for the recommended use, and containing information on maintenance rate based on endoscopic assessment, were included. The comparative efficacies of treatments were estimated by performing a Bayesian network meta-analysis, which assessed the consistency assumption. Outcomes were number or rate of patients who maintained remission.

Results: Of 4001 articles identified, 22 RCTs were eligible for analysis. One study published as an abstract was handsearched and added. The consistency hypothesis was not rejected for the analysis. The odds ratio of vonoprazan 10 mg to each PPI was 13.92 (95% credible interval [CI] 1.70–114.21) to esomeprazole 10 mg; 5.75 (95% CI 0.59–51.57) to rabeprazole 10 mg; 3.74 (95% CI 0.70–19.99) to lansoprazole 15 mg; and 9.23 (95% CI 1.17–68.72) to omeprazole 10 mg.

Conclusion: The efficacy of vonoprazan in GERD maintenance treatment may be higher than that of some PPIs. However, a direct comparison of vonoprazan and PPIs is required to confirm these effects. (Miwa, et al., 2019)

Comparison of Vonoprazan Versus Intravenous Proton Pump Inhibitor for Prevention of High-Risk Peptic Ulcers Rebleeding After Successful Endoscopic Hemostasis: A Multicenter Randomized Noninferiority Trial

Tanawat Geeratragool, Uayporn Kaosombatwattana, Arpapun Boonchote, Suvikrom Chatthammanat, Nutchanun Preechakawin, Jompol Srichot, Asawin Sudcharoen, Pavapol Sirisunhirun, Panotpol Termsinsuk, Manus Rugivarodom, Julajak Limsrivilai, Monthira Maneerattanaporn, Nonthalee Pausawasdi and Somchai Leelakusolvong

Vonoprazan vs IV PPI in High-Risk Peptic Ulcer Bleeding, Gastroenterology 2024;167:778–787

Background & Aim: High-dose proton pump inhibitor (PPI) therapy has been recommended to prevent rebleeding of high-risk peptic ulcer (PU) after hemostasis. Vonoprazan has been proven to be noninferior to PPIs in various acid-related diseases. This study aimed to compare the efficacy of vonoprazan vs PPI for preventing high-risk PU rebleeding after hemostasis.

Methods: A multicenter, randomized, noninferiority study was conducted in 6 centers. Pre-endoscopic and endoscopic therapy were performed according to standard protocol. After successful hemostasis, patients with high-risk PU bleeding (Forrest class Ia/Ib, IIa/IIb) were randomized into 1:1 to receive vonoprazan (20 mg twice a day for 3 days, then 20 mg once a day for 28 days) or high-dose PPI (pantoprazole intravenous infusion 8 mg/h for 3 days, then omeprazole 20 mg twice a day for 28 days). The primary outcome was a 30-day rebleeding rate. Secondary outcomes included 3- and 7-day rebleeding rate, all-cause and bleeding-related mortality, rate of rescue therapy, blood transfusion, length of hospital stay, and safety.

Results: Of 194 patients, baseline characteristics, severity of bleeding, and stage of ulcers were comparable between the 2 groups. The 30-day rebleeding rates in vonoprazan and PPI groups were 7.1% (7 of 98) and 10.4% (10 of 96), respectively; noninferiority (within 10% margin) of vonoprazan to PPI was confirmed (%risk difference, _3.3; 95% confidence interval, _11.2 to 4.7; P < .001). The 3-day and 7-day rebleeding rates in the vonoprazan group remained noninferior to PPI (P < .001 by Farrington and Manning test). All secondary outcomes were also comparable between the 2 groups.

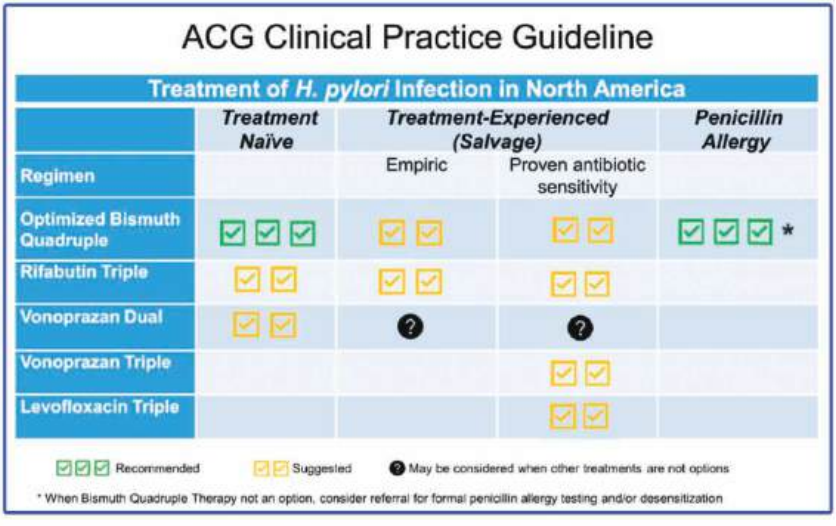
Conclusion: In patients with high-risk PU bleeding, the efficacy of vonoprazan in preventing 30-day rebleeding was noninferior to intravenous PPI. (Geeratragool, et al., 2024)

CLINICAL GUIDELINES

ACG Clinical Guideline: Treatment of Helicobacter pylori Infection

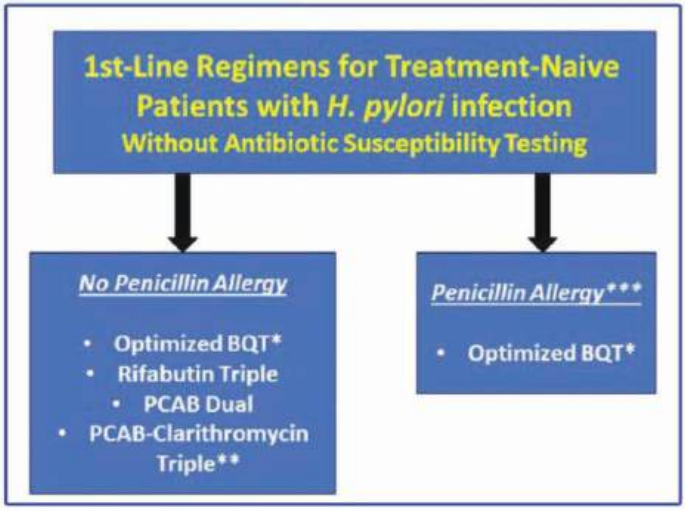
William D. Chey, MD, FACG1, Colin W. Howden, MD, FACG2, Steven F. Moss, MD, FACG3, Douglas R. Morgan, MD, MPH, FACG4, Katarina B. Greer, MD, MSEpi5, Shilpa Grover, MD, MPH6 and Shailja C. Shah, MD, MPH7

AGA Clinical Practice Update on Integrating P-CABs, Gastroenterology 2024;167:1228–1238

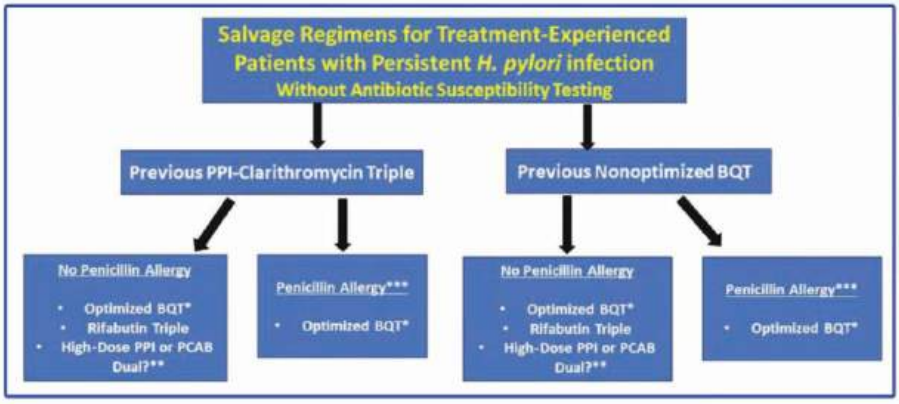


- Treatment Naïve patient with H. pylori infection, Dual Therapy with PCAB and amoxicillin is a recommended first line treatment.

- Treatment Naïve patient with H. pylori infection and unknown Clarithromycin susceptibility, PCAB-Clarithromycin Triple Therapy is suggest over PPIs Triple Therapy.



Empiric first-line regimens for treatment-naive patients with H. pylori infection (no antibiotic susceptibility testing).



Empiric salvage regimens for treatment-experienced patients with persistent H. pylori infection (no antibiotic susceptibility testing).

AGA Clinical Practice Update on Integrating Potassium-Competitive Acid Blockers Into Clinical Practice: Expert Review

Amit Patel, Loren Laine, Paul Moayyedi, and Justin Wu

Arq Gastroenterol • 2024. v. 61:e23154

Clinicians should use P-CABs in place of PPIs in eradication regimens for most patients with HP infection.

P-CABs have been studied extensively in HP treatment regimens, primarily among Asian populations. A systematic review of 7 Asian randomized trials revealed significantly higher pooled eradication rates in first-line HP treatment for vonoprazan vs PPI (92% vs 80%). It is important to note that at some of the doses studied in this context, P-CABs may not be more effective than PPIs. For example, 2 recently published studies suggested that triple therapy with tegoprazan 50 mg twice daily was not significantly more effective for HP eradication than regimens with esomeprazole 40 mg twice daily (with sodium bicarbonate) or rabeprazole 20 mg twice daily.

A duration of 14 days is generally advised for HP regimens, and US approval for vonoprazan-based regimens was for 14 days. However, P-CABs have also demonstrated efficacy as part of more streamlined treatment regimens with less medication burden and/or shorter treatment durations. A Japanese trial with 335 patients found relatively similar HP eradication rates with vonoprazan 20 mg plus amoxicillin 750 mg twice daily dual therapy for 7 days compared with vonoprazan-based triple therapy (85% vs 89%). A Singaporean trial with 244 patients compared 1 week of vonoprazan 20 mg twice daily–based triple therapy with 2 weeks of PPI-based triple therapy (omeprazole or esomeprazole or rabeprazole 20 mg twice daily) found similar rates of HP eradication (87% vs 88%).

When sub-populations of patients with clarithromycin resistant HP strains within randomized trials are assessed, P-CABs given twice daily had an even greater incremental benefit over PPI-based regimens, presumably because the increased acid inhibition that can result with the P-CAB doses used improves the efficacy of other antibiotics, such as amoxicillin.The Japanese trial cited above showed superior eradication rates for 1 week of vonoprazan dual therapy compared with vonoprazan-based triple therapy among patients with clarithromycin-resistant strains (92% vs 76%). A trial including 1046 treatment-naïve American and European adults assessed open-label dual therapy (with vonoprazan 20 mg twice daily and 1 g amoxicillin thrice daily) or double-blind triple therapy (with vonoprazan 20 mg twice daily or lansoprazole 30 mg twice daily) for 14 days. Among all study patients, HP eradication rates were superior for both vonoprazan triple therapy (81%) and dual therapy (77%) compared with lansoprazole triple therapy (69%). In particular, the vonoprazan-based regimens demonstrated markedly larger differences vs lansoprazole based regimens in eradication rates for patients with clarithromycin-resistant infections (66%–70% vs 32%). Notably, eradication rates in all arms of the trial were <90%, a threshold advised by some for eradication therapy. Regarding utility as second-line treatment, a meta-analysis of 16 Japanese studies (15 of which were retrospective) evaluating second-line HP eradication found that vonoprazan-based regimens were superior to PPI-based regimens (odds ratio, 1.5; 95% CI, 1.3–1.8).

In light of this accumulating data, the 2022 Maastricht VI/Florence Consensus featured 100% expert agreement that P-CAB–based treatment regimens for HP are "superior, or not inferior to, conventional PPI-based triple therapies . . . and superior in patients with evidence of antimicrobial resistant infections." Furthermore, in contrast to most of the other indications discussed in this Clinical Practice Update, the short-term durations of HP eradication regimens reduced potential concerns about P-CAB costs and safety in this setting. Nevertheless, further data on the optimal utility of P-CABs in HP treatment, particularly among diverse and non-Asian populations, with better understanding of the roles of susceptibility testing, antibiotic selection, and treatment dosing and durations, will be crucial for clinical guidance. (Patel, et al., 2024)

13. References

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Zifam Novocid

Brand Name	: Zifam Novocid
Generic Name	: Vonoprazan
Dosage Forms and Strengths	: 10 mg, 20 mg Tablets
Route of Administration	: Oral
Pharmacologic Class	: Potassium-competitive acid blockers (PCAB)

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