SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Gastroenterology

Dexlansoprazole Versus Esomeprazole in Concomitant Quadruple Therapy for Helicobacter Pylori Eradication: A Randomized, Open-Label, Non-Inferiority Trial

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DOI: https://doi.org/10.36347/sasjm.2026.v12i09.024 | **Received:** 11.07.2026 | **Accepted:** 21.09.2026 | **Published:** 24.09.2026

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Abstract **Original Research Article**

Background and Aims: Non-bismuth concomitant quadruple therapy is a recommended empirical first-line option for Helicobacter pylori eradication in settings where antimicrobial susceptibility is unknown or clarithromycin resistance is elevated. The proton pump inhibitor (PPI) combined with this regimen may influence eradication through its effect on intragastric acid suppression. Dexlansoprazole, a dual delayed-release PPI formulation, achieves more sustained acid suppression than esomeprazole in pharmacodynamic studies, but head-to-head data on H. pylori eradication are lacking. We aimed to determine whether dexlansoprazole is non-inferior to esomeprazole when combined with an identical 14-day concomitant quadruple regimen. ***Methods:*** In this single-center, open-label, randomized, parallel-group, non-inferiority trial conducted at the Department of Gastroenterology, Mohammed VI University Hospital, Agadir, Morocco (August 2025–August 2026), adults with confirmed H. pylori infection were randomized 1:1 to dexlansoprazole 60 mg twice daily or esomeprazole 40 mg twice daily, each combined with amoxicillin 1 g, clarithromycin 500 mg, and metronidazole 500 mg, all twice daily for 14 days. The primary outcome was eradication confirmed by urea breath test 4–6 weeks post-treatment, analyzed by intention-to-treat (ITT) and per-protocol (PP), with a pre-specified non-inferiority margin of 10 percentage points. ***Results:*** A total of 370 patients were randomized (184 dexlansoprazole, 186 esomeprazole). ITT eradication rates were 80.4% and 81.2%, respectively (risk difference −0.7%; 95% CI −8.8 to 7.3), and PP rates were 87.1% and 88.8% (difference −1.8%; 95% CI −8.7 to 5.2); both lower confidence limits exceeded the non-inferiority margin, and the result was unchanged after adjustment for a baseline imbalance in body mass index. Overall adverse-event rates were similar between arms (80.4% vs 80.1%), although diarrhea and nausea were more frequent with dexlansoprazole and abdominal pain more frequent with esomeprazole; no serious adverse events occurred. ***Conclusion:*** Dexlansoprazole was non-inferior to esomeprazole within a 14-day concomitant quadruple regimen for H. pylori eradication, with an overall comparable but qualitatively distinct tolerability profile.

Keywords: Helicobacter pylori, Non-bismuth concomitant quadruple therapy, Dexlansoprazole, Esomeprazole, Eradication rate, Non-inferiority trial.

INTRODUCTION

Helicobacter pylori infects a substantial proportion of the world's population and has been formally classified as an infectious disease. [1,2] The organism is the principal cause of chronic gastritis and a major etiological factor in peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma. [2,3] Prevalence varies markedly by region and is disproportionately high in parts of Africa, raising concerns about the adequacy of current management guidelines outside the high-income settings in which most eradication trials have been conducted. [4]

The Maastricht VI/Florence consensus recommends that treatment selection be guided by local antimicrobial susceptibility whenever possible, and that empirical non-bismuth concomitant quadruple therapy a proton pump inhibitor (PPI) combined with amoxicillin, clarithromycin, and metronidazole given concurrently be favored over legacy clarithromycin-based triple therapy in regions where clarithromycin resistance is unknown or exceeds a low single-digit threshold. [3] Pooled estimates suggest that clarithromycin resistance now affects a substantial minority of H. pylori isolates worldwide, undermining the reliability of triple therapy in many settings. [5] Reported eradication rates with 14-

day concomitant quadruple therapy have generally ranged from the low eighties to the high nineties depending on the population and background resistance profile. [6,7]

Within a quadruple regimen, the choice of PPI may itself influence eradication efficacy, because raising intragastric pH enhances both the chemical stability and the bactericidal activity of amoxicillin and clarithromycin against actively dividing H. pylori. Not all PPIs achieve equivalent or equally sustained acid suppression. Dexlansoprazole, the R-enantiomer of lansoprazole formulated with a dual delayed-release delivery system, was specifically designed to prolong the plasma concentration–time profile and extend the duration of acid suppression beyond that achieved by earlier single-release PPIs. [8] In a randomized crossover pharmacodynamic study in healthy volunteers, a single dose of dexlansoprazole 60 mg produced significantly greater 24-hour intragastric pH control than esomeprazole 40 mg, the most commonly used comparator PPI in H. pylori eradication regimens. [9]

Whether this pharmacodynamic advantage translates into a measurable difference in H. pylori eradication when dexlansoprazole is substituted for esomeprazole within an otherwise identical quadruple antibiotic regimen has not, to our knowledge, been directly examined in a randomized clinical trial. This question is particularly relevant in settings such as ours, where antimicrobial susceptibility testing for H. pylori is not routinely available and treatment is necessarily empirical, placing greater practical weight on optimizing the non-antibiotic component of the regimen. We therefore conducted a randomized, open-label, non-inferiority trial comparing dexlansoprazole with esomeprazole, each combined with an identical 14-day concomitant quadruple antibiotic regimen, hypothesizing that dexlansoprazole would be non-inferior to esomeprazole for H. pylori eradication.

METHODS

Study Design and Setting

We conducted a single-center, open-label, randomized, parallel-group, non-inferiority trial in the Department of Gastroenterology, Mohammed VI University Hospital, Agadir, Morocco, between August 2025 and August 2026.

Participants

Eligible participants were adults aged 18 years or older with active H. pylori infection confirmed by a 13C-urea breath test, fecal antigen test, or gastric histology, who provided written informed consent. Both treatment-naive patients and patients who had previously undergone unsuccessful eradication therapy were eligible for inclusion; approximately 14% of the study population had received prior eradication treatment, evenly distributed across the two arms (Table 1). Exclusion criteria were known hypersensitivity to any study drug, pregnancy or breastfeeding, severe hepatic or renal impairment, use of antibiotics or a PPI within the preceding four weeks, and prior gastric surgery.

Randomization and Interventions

Participants were assigned in a 1:1 ratio to dexlansoprazole or esomeprazole using a randomization sequence. Because the two PPI formulations differ in appearance and the trial was conducted in a pragmatic single-center setting, allocation was open-label. All participants received an identical 14-day concomitant (non-bismuth) quadruple antibiotic regimen comprising amoxicillin 1 g twice daily, clarithromycin 500 mg twice daily, and metronidazole 500 mg twice daily, administered concurrently for the full 14 days. Participants additionally received either dexlansoprazole 60 mg twice daily (experimental arm) or esomeprazole 40 mg twice daily (comparator arm) for the same duration. Antimicrobial susceptibility testing for clarithromycin or metronidazole resistance was not performed, as this testing is not routinely available at the local microbiology laboratory; treatment was therefore prescribed empirically, consistent with regional clinical practice.

Outcomes

The primary outcome was H. pylori eradication, defined as a negative urea breath test performed 4–6 weeks after completion of treatment, with PPI therapy withheld for at least two weeks before testing to minimize the risk of a false-negative result. Eradication was analyzed in the intention-to-treat (ITT) population (all randomized participants, with participants lost to follow-up classified as treatment failures) and in the per-protocol (PP) population (participants who completed the full 14-day regimen and underwent post-treatment testing). Secondary outcomes were self-reported treatment adherence (percentage of prescribed doses taken), adverse events (graded by severity and assessed for causality), and change in gastrointestinal symptom burden measured with the Gastrointestinal Symptom Rating Scale (GSRS), a validated 15-item instrument covering reflux, abdominal pain, indigestion, diarrhea, and constipation, administered before treatment and at the post-treatment visit.

Sample Size

Assuming a reference eradication rate of 90%, a non-inferiority margin of 10 percentage points, 80% power, and a one-sided alpha of 0.025 consistent with regulatory conventions for non-inferiority trials 142 evaluable participants per arm were required. Anticipating 15% loss to follow-up, a total sample size of 340 participants (170 per arm) was targeted.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation and compared using the Mann-Whitney U test; categorical variables were compared

using the chi-square test or Fisher's exact test as appropriate. The between-group difference in eradication rates and its 95% confidence interval (CI) were estimated using the Wald method for the difference between two independent proportions. Non-inferiority was declared if the lower bound of the 95% CI for the risk difference (dexlansoprazole minus esomeprazole) exceeded the pre-specified margin of −10 percentage points. A pre-planned sensitivity analysis addressing an observed imbalance in baseline body mass index (BMI) used multivariable logistic regression (eradication ~ treatment arm + BMI) followed by standardization to estimate an adjusted risk difference, with 95% CIs derived from 2,000 bootstrap resamples. A two-sided p-value <0.05 was considered statistically significant for all comparisons other than the pre-specified one-sided non-inferiority comparison. Analyses were performed in Python (pandas, SciPy, statsmodels).

Ethics

The study was conducted in accordance with the Declaration of Helsinki. [Ethics committee approval reference to be inserted prior to submission.] All participants provided written informed consent before enrollment.

RESULTS

Between August 2025 and August 2026, 370 patients were randomized: 184 to dexlansoprazole and 186 to esomeprazole (Figure 1). Baseline demographic and clinical characteristics were well balanced between arms, with the exception of BMI, which was higher in the dexlansoprazole arm (23.4 ± 3.5 vs 22.1 ± 2.2 kg/m²; p<0.001) (Table 1).

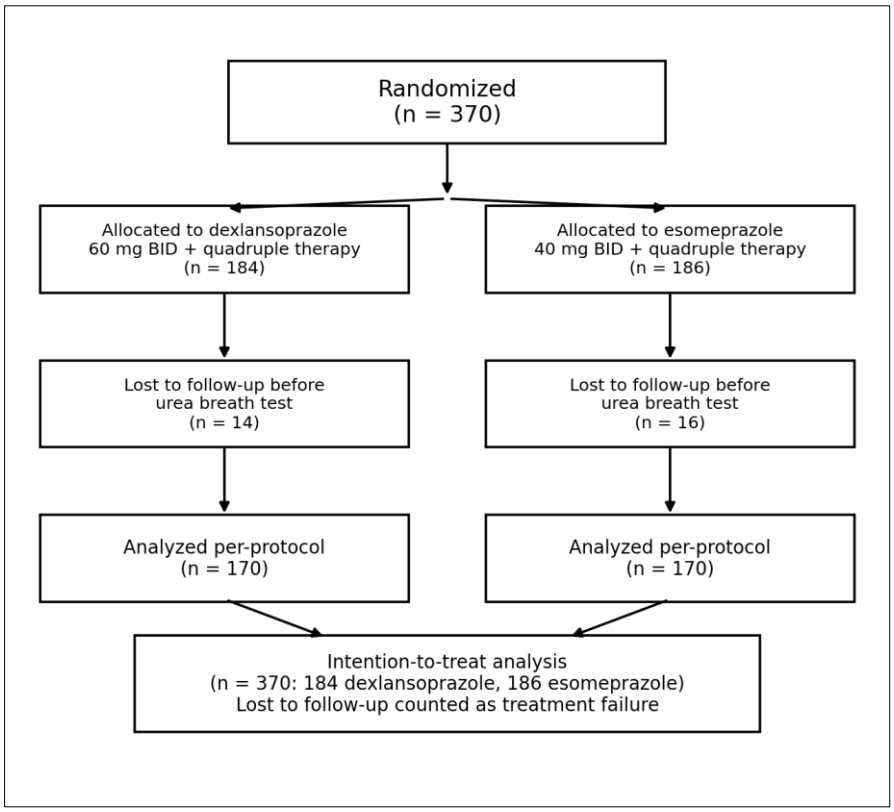

Figure 1: Patient flow through the trial

Table 1: Baseline characteristics by treatment arm

Characteristic	Dexlansoprazole (n=184)	Esomeprazole (n=186)	p
Age, years, mean ± SD	42.5 ± 13.1	44.4 ± 13.7	0.230
Female sex, %	~46	~50	0.601
Body mass index, kg/m², mean ± SD	23.4 ± 3.5	22.1 ± 2.2	**<0.001***
Current smoker, %	~38	~35	0.687
Alcohol use, %	~12	~7	0.070
Known peptic ulcer disease, %	~7	~6	0.979
NSAID/aspirin use, %	~17	~14	0.364
Prior eradication therapy, %	~14	~13	1.000
Baseline GSRS score, mean ± SD	15.6 ± 4.1	16.2 ± 3.9	0.345

Primary Outcome

In the ITT population, eradication was achieved in 148/184 (80.4%) dexlansoprazole recipients and 151/186 (81.2%) esomeprazole recipients, a risk difference of −0.7 percentage points (95% CI −8.8 to 7.3) (Table 2). Because the lower bound of this interval exceeded the pre-specified non-inferiority margin of −10%, dexlansoprazole met the criterion for non-inferiority in the primary ITT analysis.

Table 2: Primary outcome intention-to-treat analysis

	Dexlansoprazole	Esomeprazole
Randomized, n	184	186
Eradication confirmed, n	148	151
Confirmed treatment failure, n	22	19
Lost to follow-up (counted as failure), n	14	16
Eradication rate, % (95% CI)	80.4 (74.1–85.5)	81.2 (75.0–86.1)
Risk difference (95% CI)	−0.7% (−8.8 to 7.3)	

In the PP population (170 evaluable participants per arm, following exclusion of 30 participants lost to follow-up), eradication rates were 87.1% and 88.8%, respectively (difference −1.8%; 95% CI −8.7 to 5.2), again meeting the non-inferiority criterion (Table 3).

Table 3: Primary outcome per-protocol analysis

	Dex lansoprazole	Esomeprazole
Evaluable, n	170	170
Eradication confirmed, n (%)	148 (87.1)	151 (88.8)
Confirmed treatment failure, n (%)	22 (12.9)	19 (11.2)
Risk difference (95% CI)	−1.8% (−8.7 to 5.2)	

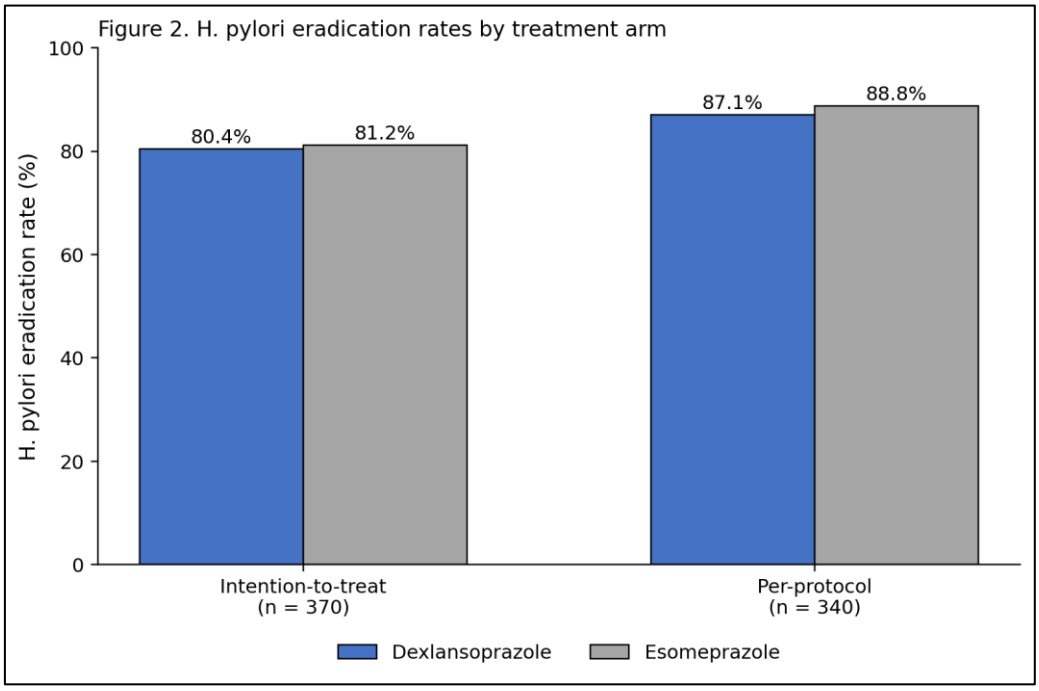

Figure 2: H. pylori eradication rates by treatment arm and analysis population

Sensitivity Analysis

Adjustment for baseline BMI yielded an adjusted risk difference of −1.2% (95% CI −9.3 to 6.8) in the ITT population and −1.9% (95% CI −8.4 to 5.3) in the PP population, materially unchanged from the unadjusted estimates (Table 5, Figure 3). BMI was not significantly associated with eradication success in the adjusted model (p=0.58), and the adjusted odds ratio for treatment arm (0.92, 95% CI 0.54–1.57; p=0.77) closely approximated the crude estimate, indicating that the baseline BMI imbalance did not confound the primary comparison.

Table 5: Sensitivity analysis adjusted for body mass index

Analysis	Crude risk difference	BMI-adjusted risk difference
Intention-to-treat	−0.7% (−8.8 to 7.3)	−1.2% (−9.3 to 6.8)
Per-protocol	−1.8% (−8.7 to 5.2)	−1.9% (−8.4 to 5.3)

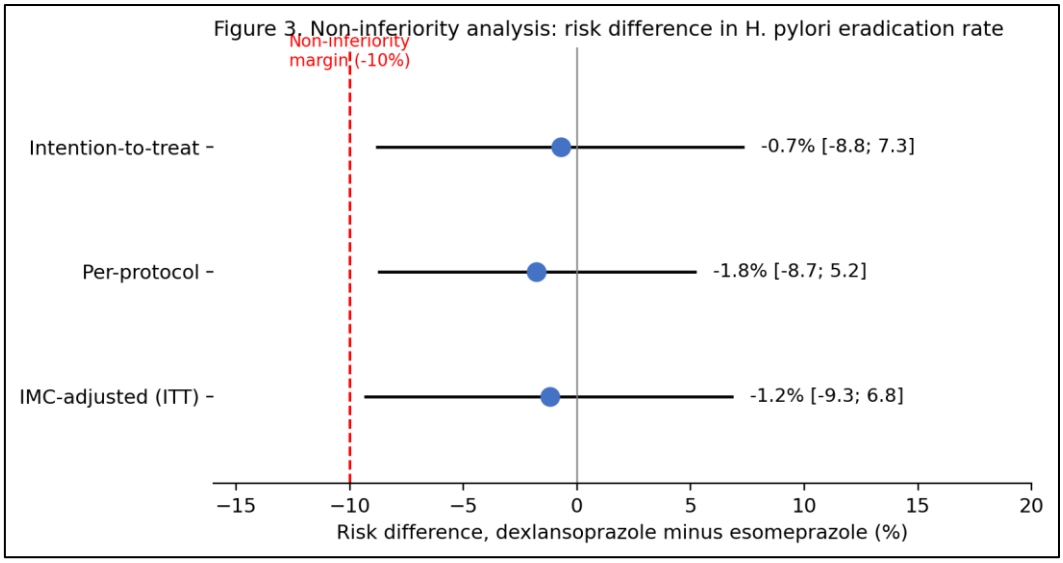

Figure 3: Risk difference in eradication rate (dexlansoprazole minus esomeprazole) across analysis populations, relative to the pre-specified non-inferiority margin

Secondary Outcomes

At least one adverse event was reported by 148/184 (80.4%) dexlansoprazole recipients and 149/186 (80.1%) esomeprazole recipients (p=1.00). Diarrhea (19.6% vs 10.2%; p=0.013) and nausea (8.7% vs 1.6%; p=0.002) were significantly more frequent with dexlansoprazole, whereas abdominal pain was more frequent with esomeprazole (46.2% vs 64.0%; p=0.001). Vomiting occurred at similar rates in both arms, and no serious adverse events were recorded (Table 4). Self-reported adherence was high and did not differ between arms (97.0% ± 1.5 vs 97.0% ± 1.7; p=0.87). Among evaluable participants, the mean GSRS score fell from 15.5 to 2.9 in the dexlansoprazole arm and from 16.3 to 3.2 in the esomeprazole arm (both p<0.0001 for within-group change), with no significant between-group difference in the magnitude of improvement.

Table 4: Adverse events by treatment arm

Adverse event	Dex lansoprazole (n=184)	Esomeprazole (n=186)	p
At least one adverse event, n (%)	148 (80.4)	149 (80.1)	1.000
Diarrhea, n (%)	36 (19.6)	19 (10.2)	**0.013***
Nausea, n (%)	16 (8.7)	3 (1.6)	**0.002***
Abdominal pain, n (%)	85 (46.2)	119 (64.0)	**0.001***
Vomiting, n (%)	9 (4.9)	7 (3.8)	0.620
Serious adverse event, n (%)	0 (0)	0 (0)	—

DISCUSSION

In this randomized, open-label, non-inferiority trial, dexlansoprazole was non-inferior to esomeprazole when combined with an identical 14-day concomitant quadruple antibiotic regimen for H. pylori eradication. This conclusion was consistent across the intention-to-treat and per-protocol analyses and was unchanged after adjusting for a baseline imbalance in BMI, with all point estimates for the risk difference clustering within two percentage points of zero and comfortably clear of the pre-specified 10-percentage-point margin. This convergence across three related but not fully independent analyses strengthen confidence that the finding reflects true comparability between the two PPIs rather than a result specific to any single analytical approach.

Our per-protocol eradication rates (87.1% and 88.8%) closely resemble those reported for 14-day non-bismuth concomitant quadruple therapy in comparable settings; Yadollahi and colleagues reported an 88.6% per-protocol eradication rate with a pantoprazole-based 14-day concomitant regimen in a population with high background antibiotic resistance, alongside an intention-to-treat rate of 81.6%, closely matching the 80–81% ITT rates observed in our cohort.[6] Considerably higher eradication rates, in some cases exceeding 95%, have been reported for 14-day concomitant regimens in

settings that incorporated susceptibility-guided antibiotic selection.[7] Taken together, this pattern suggests that the moderate eradication rates observed here most plausibly reflect background antimicrobial resistance and the empirical nature of treatment selection at our center, rather than an inherent limitation of either PPI evaluated.

The absence of a measurable eradication advantage for dexlansoprazole is noteworthy given pharmacodynamic evidence that a single dose of dexlansoprazole achieves greater and more sustained 24-hour intragastric pH control than esomeprazole.[8,9] A plausible explanation is a ceiling effect: once intragastric pH is raised sufficiently to stabilize amoxicillin and to render H. pylori metabolically active and susceptible to clarithromycin, further incremental gains in acid suppression may contribute little additional benefit to eradication, which is likely to be more strongly determined by antimicrobial susceptibility, antibiotic exposure, and treatment adherence than by modest differences in acid-suppression intensity between two already highly potent PPIs.

The qualitative difference in adverse-event profile between arms more diarrhea and nausea with dexlansoprazole, more abdominal pain with esomeprazole is a hypothesis-generating observation rather than a mechanistically established finding, and should be interpreted cautiously given the open-label design and the recording of only a single predominant adverse event per participant, which precluded a fully granular safety analysis. Overall tolerability, reflected in the similar proportion of participants reporting at least one adverse event and the absence of serious adverse events in either arm, was reassuring for both agents.

This trial has several strengths, including a randomized design with a formally calculated sample size, concordant conclusions across intention-to-treat and per-protocol analyses, a pre-specified sensitivity analysis addressing a baseline covariate imbalance, and transparent data-quality procedures: several data-entry discrepancies identified during data cleaning, including a treatment-arm misclassification affecting three participants and an isolated treatment-duration entry error, were corrected against source records before the final analysis reported here.

Several limitations should be acknowledged. The open-label design may have introduced reporting bias for patient-reported outcomes such as symptoms and adverse events. The single-center design may limit generalizability to other populations and resistance settings. Antimicrobial susceptibility testing for clarithromycin and metronidazole was not available, precluding an assessment of whether resistance patterns differentially affected the two arms; this is a substantive limitation given that approximately 14% of participants had previously undergone unsuccessful eradication therapy, a population generally associated with lower retreatment success, and treatment-naive and previously-treated participants were not analyzed separately. The pre-trial sample-size calculation assumed a 90% reference eradication rate, whereas the rate actually observed in the comparator arm was closer to 81% in intention-to-treat analysis; this discrepancy widened the achieved confidence intervals beyond those anticipated at the design stage, although the non-inferiority margin was nonetheless met. Finally, this trial was not prospectively registered in a public clinical trials registry, a limitation the author acknowledges and intends to address in future studies.

These findings suggest that dexlansoprazole is a reasonable therapeutic alternative to esomeprazole for centers relying on empirical concomitant quadruple therapy for H. pylori eradication. Multicenter, blinded trials incorporating antimicrobial susceptibility testing and more granular multi-event safety recording would help confirm these findings and further characterize the differential tolerability signals observed here.

CONCLUSION

In this randomized, open-label, non-inferiority trial, dexlansoprazole was non-inferior to esomeprazole when combined with a 14-day concomitant quadruple regimen for Helicobacter pylori eradication, with concordant results across intention-to-treat, per-protocol, and BMI-adjusted analyses. Overall tolerability was comparable between the two agents, although the qualitative adverse-event profile differed. These findings support dexlansoprazole as an effective alternative proton pump inhibitor for H. pylori eradication therapy in similar clinical settings, pending confirmation in larger, multicenter, blinded trials.

REFERENCES

1. Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, *et al.,*Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology. 2017;153(2):420-429.
2. Malfertheiner P, Camargo MC, El-Omar E, Liou JM, Peek R, Schulz C, *et al.,*Helicobacter pylori infection. Nat Rev Dis Primers. 2023;9(1):19.
3. Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, et al.; European Helicobacter and Microbiota Study Group. Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. Gut. 2022;71(9):1724-1762.
4. Setshedi M. Is the current Maastricht consensus report applicable for H. pylori management in sub-Saharan Africa? Dig Dis. 2023;41(4):572-573.
5. Sholeh M, Khoshnood S, Azimi T, Mohamadi J, Kaviar VH, Hashemian M, *et al.,*The prevalence of clarithromycin-resistant Helicobacter pylori isolates: a systematic review and meta-analysis. PeerJ. 2023;11:e15121.

6. Yadollahi B, Valizadeh Toosi SM, Bari Z, Fakheri H, Maleki I, Taghvaei T, *et al.,*Efficacy of 14-day concomitant quadruple therapy and 14-day high-dose dual therapy on H. pylori eradication. Gastroenterol Hepatol Bed Bench. 2022;15(2):172-178.
7. Amiot A, *et al.,*14-day tailored PCR-guided triple therapy versus 14-day non-bismuth concomitant quadruple therapy for Helicobacter pylori eradication: a multicenter, open-label randomized noninferiority controlled trial. Helicobacter. 2024.
8. Metz DC, Vakily M, Dixit T, Mulford D. Review article: dual delayed release formulation of dexlansoprazole MR, a novel approach to overcome the limitations of conventional single release proton pump inhibitor therapy. Aliment Pharmacol Ther. 2009;29(9):928-937.
9. Kukulka M, Eisenberg C, Nudurupati S. Comparator pH study to evaluate the single-dose pharmacodynamics of dual delayed-release dexlansoprazole 60 mg and delayed-release esomeprazole 40 mg. Clin Exp Gastroenterol. 2011;4:213-220.
10. Svedlund J, Sjödin I, Dotevall G. GSRS—a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. Dig Dis Sci. 1988;33(2):129-134.
11. International Conference on Harmonisation. ICH Harmonised Tripartite Guideline: Statistical Principles for Clinical Trials (E9). 1998.
12. Chen PY, Tsai FP, Chen MJ, Yang HY, Wu MS, Liou JM. Vonoprazan-based versus proton pump inhibitor-based therapy in Helicobacter pylori eradication: an updated systematic review and meta-analysis of randomised trials. Gut. 2024;73(5):872-874.