CURSO DE AVANCES EN GASTROENTEROLOGÍA
PERSPECTIVAS FUTURAS EN GASTROENTEROLOGÍA
17 - 19 Julio 2024 - Hotel InterContinental, Stgo.
SChGE

UC | Chile

Lo Mejor de la DDW 2024: Novedades en *Helicobacter pylori*

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Sociedad Chilena de Gastroenterología

Introducción

Helicobacter pylori (HP):

- Gram (-) flagelada
- Microaerófila
- Sobrevive en la acidez gástrica
- Coloniza la mucosa gástrica
- Desde Este de África hace 60.000 años
- Conocido científicamente en 1983
- **Carcinógeno tipo I (OMS) 1994**

Introducción

- *Se* asocia a enfermedades prevalentes: Gastritis crónica, úlcera péptica, linfoma de MALT y cáncer gástrico.
- Cáncer gástrico: una de las principales causas de muerte en hombres y mujeres en América Latina.
- **En América Latina, la infección por *H. pylori* tiene una alta prevalencia (47-63%).**
- Las indicaciones de erradicación, las pruebas diagnósticas y los esquemas utilizados, son altamente heterogéneos entre los países.

Prevalencia de infección por H. pylori

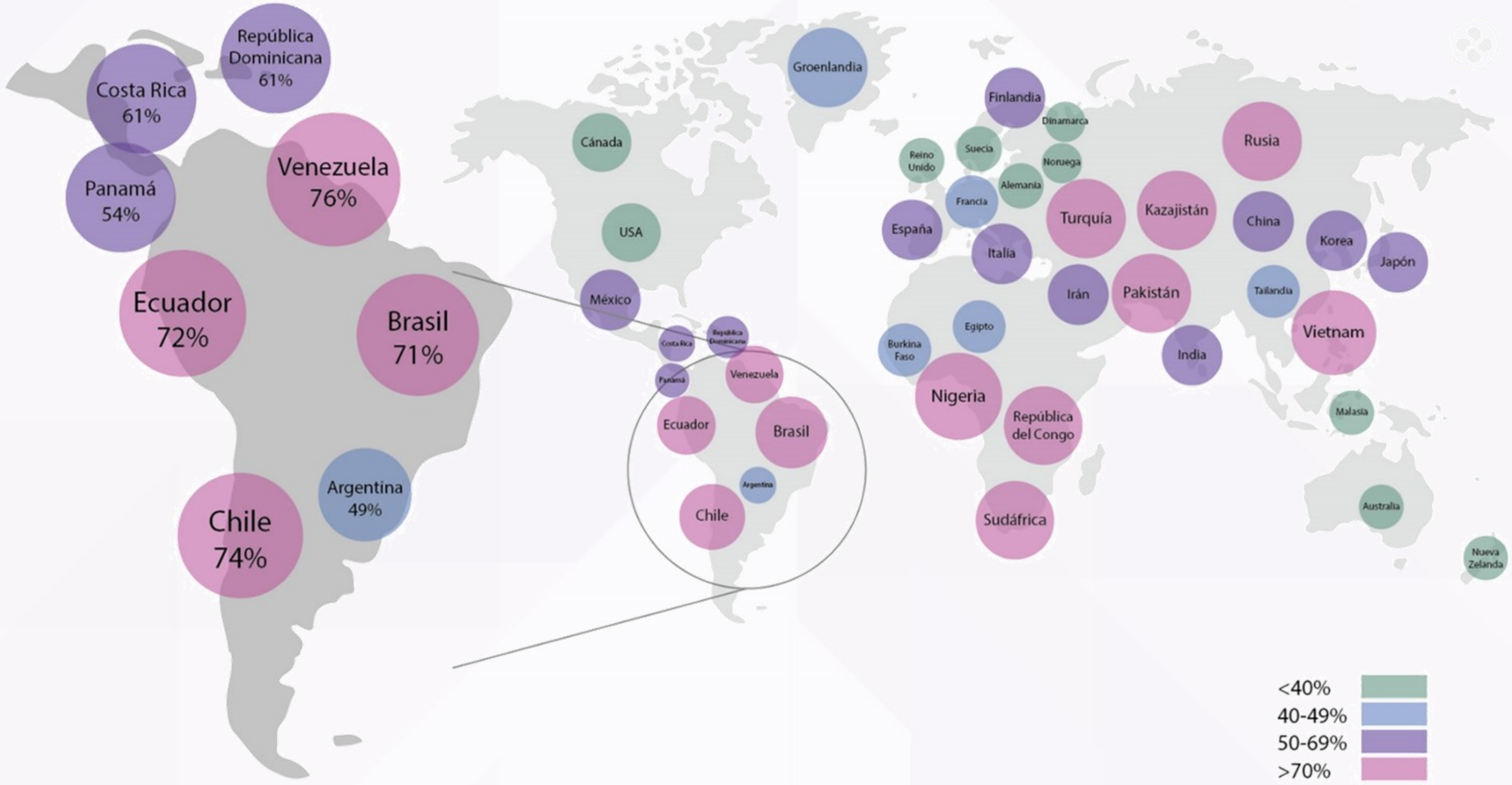
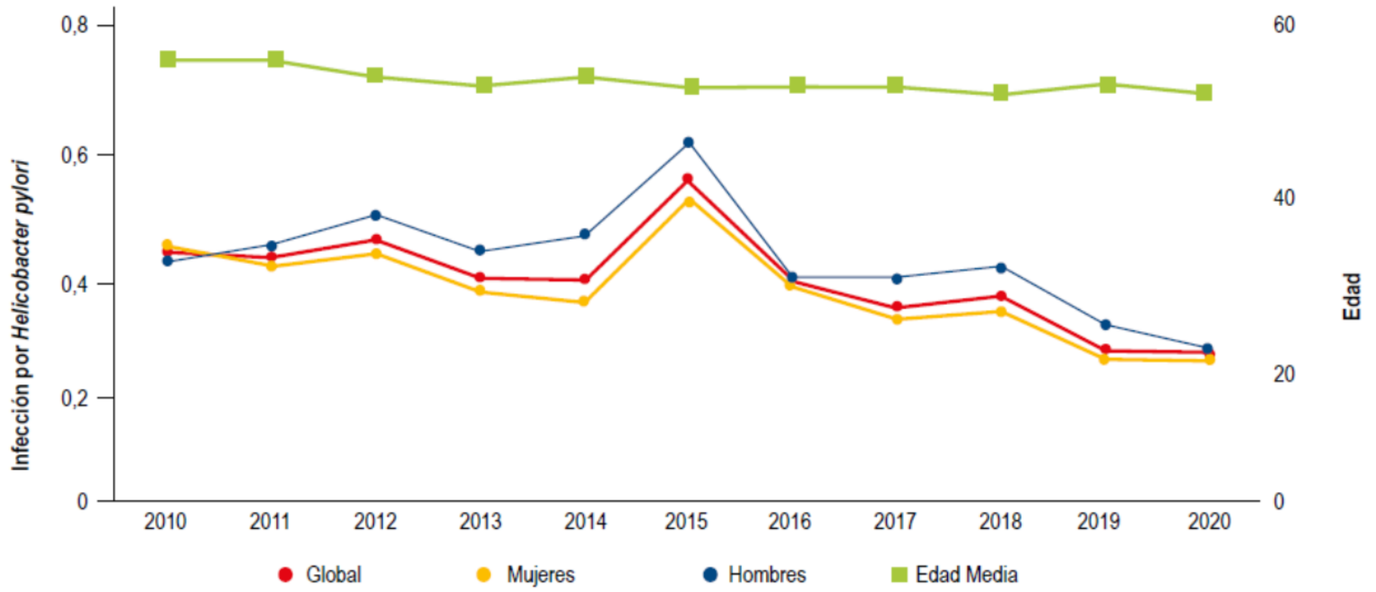


Imagen: Valentina Riquelme
Adaptado de: Gastroenterología y Hepatología Clínica 2020. ISBN 978-956-220-424-8

Prevalencia de H. pylori en Chile

Reducción de la infección por *Helicobacter pylori* en pacientes derivados a endoscopia digestiva alta en Santiago de Chile entre 2010-2020



Año	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Frecuencia de *Helicobacter pylori*, n(%)	458 (45,1)	493 (44,1)	498 (46,9)	576 (41,1)	611 (40,8)	586 (56)	488 (40,3)	286 (36,6)	298 (38,5)	264 (30,1)	167 (29)

Figura 1. Frecuencia de infección por *Helicobacter pylori* (*Hp*) en pacientes que asisten a una primera endoscopia digestiva alta ambulatoria entre el año 2010-2020.

Rev Gastroenterol Peru 2024;44(1):14-20

Think tank NIH

Se realizó un meeting precongreso en NIH/NCI para prevención del cáncer gástrico a nivel global.
Las novedades incluyeron:

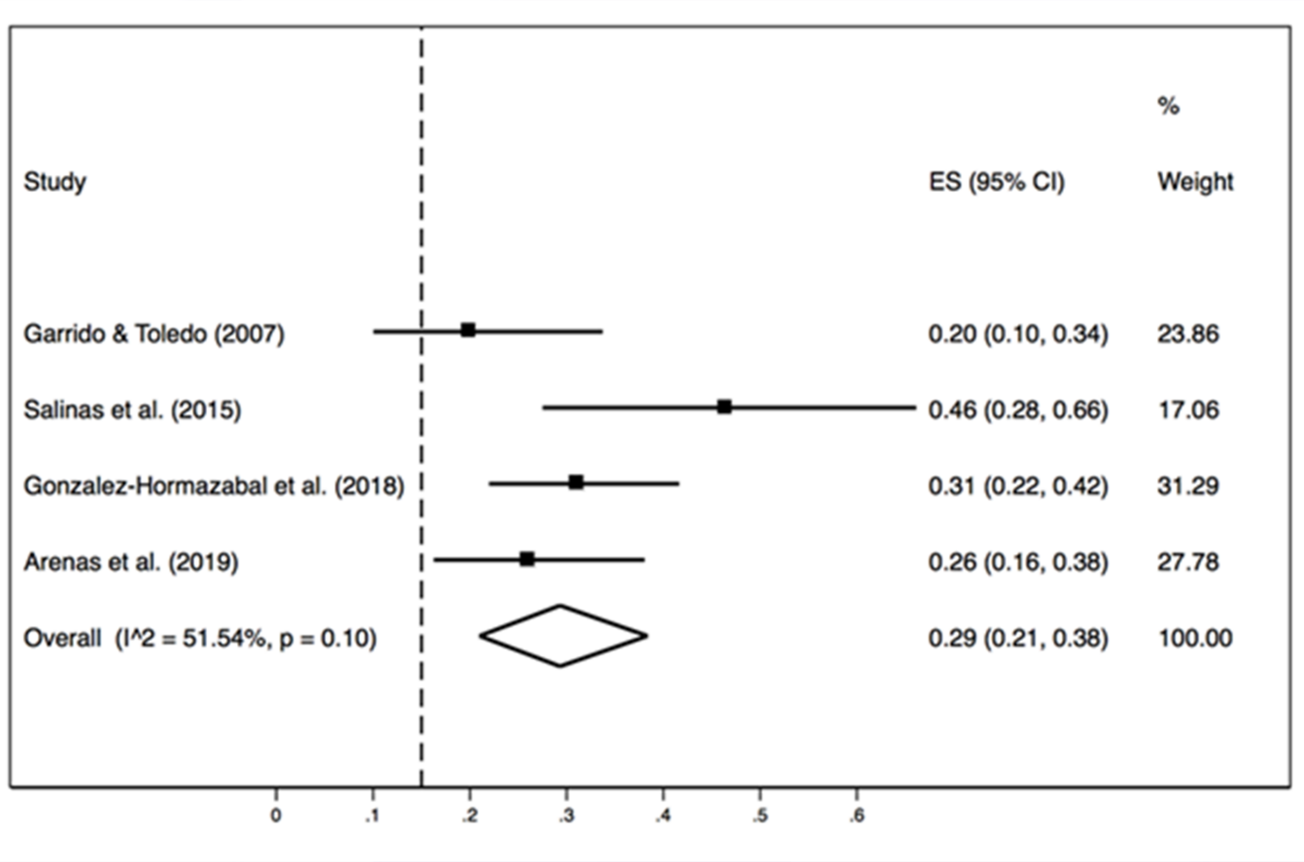
- Propuesta de prevención primaria del cáncer gástrico a través de erradicación masiva (test and treat).
- Desarrollo de vacuna por parte de un grupo alemán que estaría disponible para pruebas en humanos en 4 años más.

Prevalencia de resistencia a ATB

SCIENTIFIC REPORTS
nature research

OPEN

High prevalence of clarithromycin resistance and effect on Helicobacter pylori eradication in a population from Santiago, Chile: cohort study and meta-analysis



Scientific Reports 2019;9(1):20070.

Prevalencia de resistencia a ATB

Prevalence of *Helicobacter pylori* Antimicrobial Resistance Among Patients Recruited in Endoscopy Units in Santiago, Chile

Age ($n=143$)	Levofloxacin-Resistant Prevalence (95% CI)	OR (95% CI)	p	Clarithromycin-Resistant Prevalence (95% CI)	OR (95% CI)	p
<40 years ($n=53$)	16.1%	1 (reference)	–	19.6%	1 (reference)	-
40–49 years ($n=28$)	26.9%	1.82 (0.60–5.59)	0.290	26.9%	1.51 (0.51–4.48)	0.460
50–60 years ($n=32$)	40.0%	3.48 (1.25–9.66)	0.017*	30.0%	1.75 (0.63–4.87)	0.282
>60 years ($n=30$)	41.9%	3.77 (1.38–10.34)	0.010*	38.7%	2.58 (0.97–6.87)	0.057
p value	0.026[a]		0.004[b]	0.278[†]		0.057[‡]

[a]Fisher's exact test, [b]Wald's test. Statistically significant odds ratio (OR) in bold, *p value<0.05. CI: confidence interval.

>60 yo: Levofloxacin resistance (41.9%) and Claritromycin (38.7%)

NGS *H. pylori* AB resistance:
(n=164 in Santiago, Chile)

CLA	**39.5%**
FLU	**33.6%**
MTZ	**34.2%**
AMOX	**2.7%**
TETRA	**0.0%**
RFB	**0.7%**

Ongoing multicentric Latam study:
México, Colombia, Ecuador, Perú, Argentina, Uruguay and Chile

Gonzalez P, et al. Arch Medical Res 2021;52:529-534

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HpLATAM-Reg

Hp - Latam Reg

Helicobacter pylori Latin-American Registry

Latin American Registry on the Management of *Helicobacter pylori* Infection (HpLATAM-Reg)

WorldHpReg

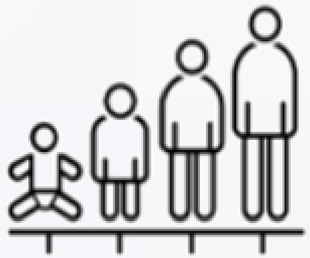
Worldwide Registry on the management of Helicobacter pylori

OPGE

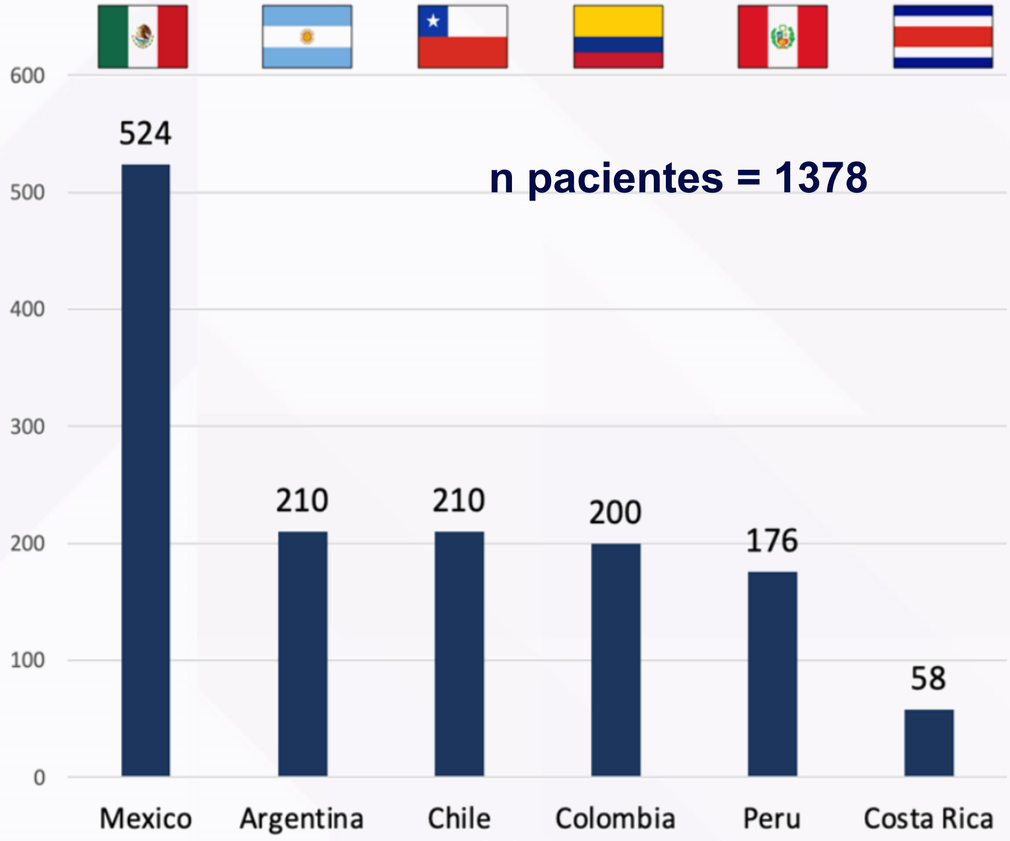
AEG

HpLATAM-Reg

68% / 32%



Mean (SD)
53 (14) years of age



n pacientes = 1378

HpLATAM-Reg

Table 1. Main characteristics of the patients	
Characteristics	**Descriptive statistics (n=681)**
Average age	51 years (SD 15.2)
Sex	459 women (67%)
Indication of treatment	
Non-investigated Dyspepsia	44% (n=296)
Dyspepsia with normal endoscopy	22% (n=147)
Duodenal Ulcer	3.2% (n=22)
Gastric Ulcer	4.1% (n=28)
Preneoplastic lesions	1% (n=7)
MALT Lymphoma	0.7% (n=5)
First-degree relatives of patients with gastric cancer	0.3% (n=2)
Unexplained iron deficiency anaemia	0.1% (n=1)
Idiopathic thrombocytopenic purpura	0.6% (n=4)
No data	0.1% (n=1)
Number of previous eradications	
Naïve (no previous treatment)	88% (n=599)

Inclusion criteria	Exclusion criteria
- Patients older than 18 years. - Diagnosed with *H. pylori* infection. - In treatment with a eradication therapy defined for the treating physician.	- No confirmatory eradication test.

HpLATAM-Reg

Table 2. Diagnostic tests before eradication	
Non-invasive tests	20% (n=138)
^{13}C UBT	15% (n=102)
^{14}C UBT	2.3% (n=16)
Serology	0%
SA Monoclonal Test	2.1% (n=14)
SA Polyclonal Test	0.9% (n=6)
Invasive tests	80% (n=542)
Histology	55.9% (n=381)
RUT	24% (n=161)
Culture	0%
No test performed	0.1% (n=1)
The number of tests is not equal as the number of patients because more than one test could be conducted. UBT = Urea Breath Test; SA = Stool Antigen; RUT = Rapid Urease Test.	

HpLATAM-Reg

Table 3. Most commonly used first-line eradication therapies for *H. pylori* infection in Latin America, by length of treatment and proton pump inhibitor dose.					
Prescriptions, n (%)	**PPI-C-A** **272 (46%)**	**PPI-C-A-M** **107 (18%)**	**PPI-A** **44 (7%)**	**PPI-C-A-B** **36 (6%)**	**PPI-A-L** **33 (6%)**
Length of treatment					
7 days	6 (2.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
10 days	17 (6.3%)	1 (0.9%)	1 (2.3%)	0 (0%)	5 (15.2%)
14 days	246 (91.4%)	106 (99.1%)	43 (97.7%)	36 (100%)	28 (84.8%)
PPI dose*					
Low	167 (61.6%)	42 (39.3%)	1 (2.3%)	13 (36.1%)	14 (45.2%)
Standard	34 (12.5%)	10 (9.3%)	3 (6.8%)	9 (25%)	1 (3.2%)
High	70 (25.8%)	55 (51.4%)	40 (90.9%)	14 (38.9%)	16 (51.6%)
mITT effectiveness	79.8% of 272	90.7% of 107	86.4% of 44	80.6% of 36	72.7% of 33
A: amoxicillin; B: bismuth; C: clarithomycin; L: levofloxacin, M: metronidazole; PPI: proton pump inhibitor; * Low dose PPI – 4.5 to 27 mg omeprazole equivalents. b.i.d.; standard dose PPI – 32 to 40 mg omeprazole equivalents. b.i.d.; high dose PPI – 54 to 128 mg omeprazole equivalents. b.i.d.					

Terapia cuádruple vs. triple estándar

Terapias cuádruples son superiores a terapia triple-estándar en primera línea de erradicación de *H. pylori* en Chile

Tabla 2 Comparación de la tasa de efectividad de triple terapia estándar con terapia dual, concomitante y cuádruple con bismuto

Esquema	Tasa de erradicación (%) (IC 95%)	Riesgo relativo (IC 95%)	Valor p
Triple terapia estándar (n = 133)	81,95 (74,44-87,63)	Referencia	
Terapia dual (n = 35)	88,57 (73,13-95,67)	1,08 (0,94-1,25)	0,288
Terapia concomitante (n = 32)	93,75 (78,07-98,44)	1,14 (1,01-1,29)	0,028
Terapia cuádruple con bismuto (n = 42)	97,62 (84,81-99,67)	1,19 (1,09-1,31)	< 0,001

¿Qué hago el 2024?
Ajusto amoxicilina a 50 mg/Kg

Reyes D, et al. Gastroenterología y Hepatología 2022.

Terapia cuádruple vs. triple estándar

Inclusion criteria

Diagnosed with H. *pylori* infection;
receiving eradication treatment as STT, QCT, or QBT;
with an eradication test at least one month after treatment.

Statistical analysis

Descriptive Statistics, eradication rates; poisson multilevel multivariate regressions

Main Findings

1. Eradication rates STT:75.2%; QCT:88.7%; QBT:91.3%.
2. QCT and QBT, both with and without bismuth, had higher adjusted treatment success.
3. QBT achieved an eradication rate over 90%, reaching the desired threshold of optimal therapeutic eradication

Gastroenterol Hepatol 2022 Aug-Sep;45(7):515-523

Nuevas terapias disponibles

Gastroenterology 2017;152:706–715

AGA CLINICAL PRACTICE UPDATE: EXPERT REVIEWS

The Risks and Benefits of Long-term Use of Proton Pump Inhibitors: Expert Review and Best Practice Advice From the American Gastroenterological Association

Daniel E. Freedberg,[1] Lawrence S. Kim,[2] and Yu-Xiao Yang[3]

[1]Division of Digestive and Liver Diseases, Columbia University Medical Center, New York, New York; [2]South Denver Gastroenterology, P.C., Littleton, Colorado; [3]Divison of Gastroenterology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

Clinical Study

Vonoprazan-Based Regimen Is More Useful than PPI-Based One as a First-Line *Helicobacter pylori* Eradication: A Randomized Controlled Trial

Masafumi Maruyama,[1] Naoki Tanaka,[2] Daisuke Kubota,[1] Masayuki Miyajima,[1] Takefumi Kimura,[1] Koujiro Tokutake,[1] Ryujiro Imai,[1] Toru Fujisawa,[1] Hiromitsu Mori,[1] Yoshiaki Matsuda,[1] Shuichi Wada,[1] Akira Horiuchi,[3] and Kendo Kiyosawa[4]

Bloqueador competitivo de potasio: Vonoprazan/Tegoprazan
400 veces más potente que esomeprazol; aumenta efectividad 77% a 88% Japón.
Maastricht VI recomienda terapia dual con Vonoprazan, cuando esté disponible, e indica que se han reportado terapias altamente eficaces de Vonoprazan-amoxicilina.

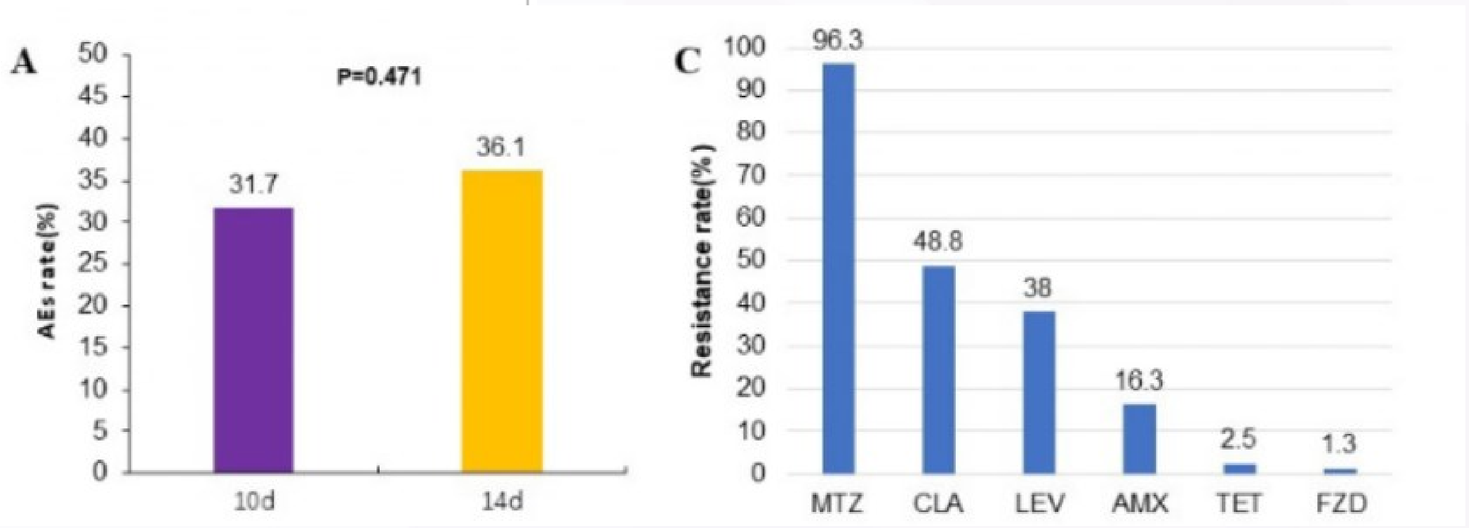
Ten-versus Fourteen-Day Vonoprazan and High-dose Amoxicilin Dual-Therapy for *Helicobacter pylori* erradication

Table 1. Eradication rate of each treatment group

Analysis	Group A	Group B	p value	Difference from group B (adjusted 95%CI for difference)
ITT	89.60% (112/125)	91.20% (114/125)	0.668	-1.60%(-5.96%-9.21%)
ITT 95%CI	83.02%-93.82%	84.93%-95.02%		
MITT	91.06% (112/123)	93.44% (114/122)	0.485	-2.39% (-4.63%-9.51%)
MITT 95%CI	84.70%-94.94%	87.59%-96.64%		
PP	91.67% (110/120)	93.39% (113/121)	0.6115	-1.72% (-5.26-8.82%)
PP 95%CI	85.34%-95.41%	87.50%-96.61%		

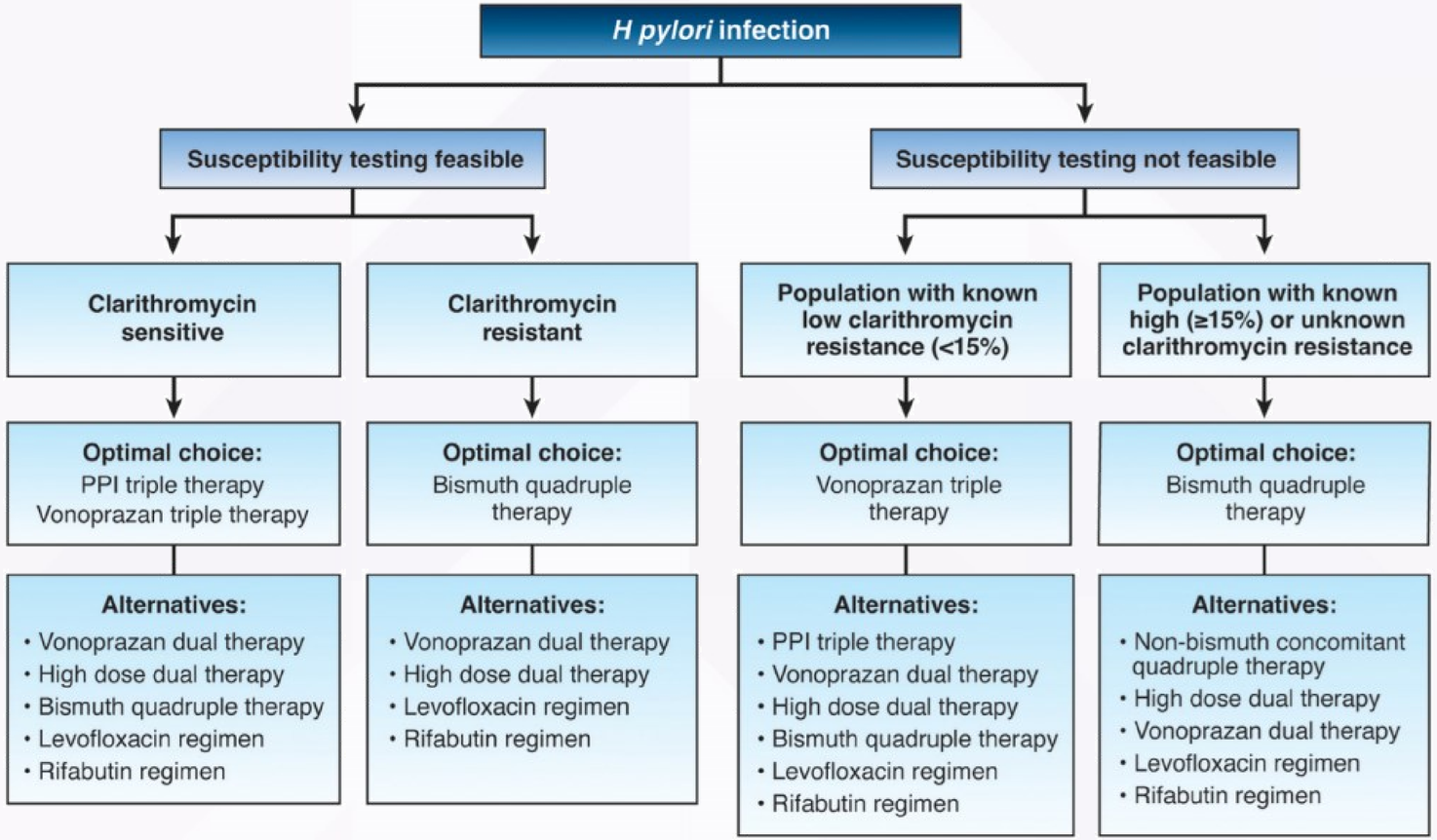
Group A, vonoprazan and high-dose amoxicillin dual therapy, 10d.
Group B, vonoprazan and high-dose amoxicillin dual therapy, 14d.

Esquema de 14 días con vonoprazan tiene 96% de tasa de erradicación para una resistencia a AMX de 16%.



Lin A, et al. Presentado en DDW 2024

The Current Role of Vonoprazan in *Helicobacter pylori* Treatment



Fallone C, et al. Gastroenterology 2022;163:572–585

PCAB's vs PPI

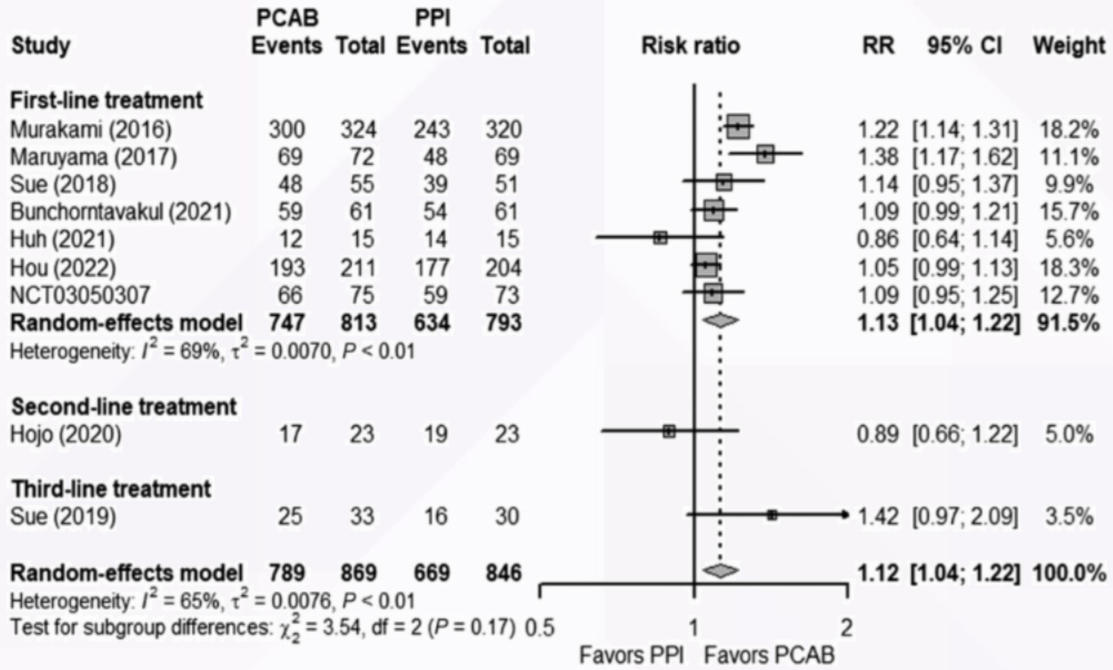


Figure 4 Forest plots comparing the eradication rates of *Helicobacter pylori* in patients receiving Vonoprazan and PPI as first-line, second-line, and third-line treatment. The RR and 95% CI for each study are presented in logarithmic scale. The pooled RRs are derived from the random-effects model. CI, confidence interval; PCAB, potassium-competitive acid blocker; PPI, proton pump inhibitor; RR, risk ratio.

Simadibrata D, et al. J Gastroenterol Hepatol 2022;37:2217-2228

Tegoprazan

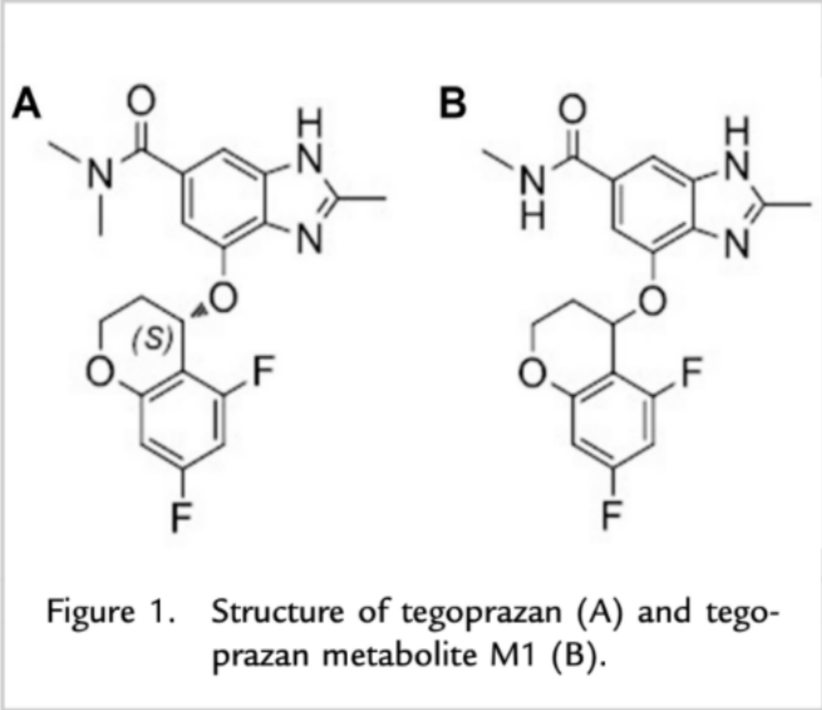


Figure 1. Structure of tegoprazan (A) and tegoprazan metabolite M1 (B).

Table IV. Pharmacokinetic parameters of metronidazole, tetracycline, and bismuth after multiple oral administrations with or without tegoprazan (N = 10). Values are presented as the mean (SD), except for T_{max} values presented as median [minimum–maximum].

Parameter	Coadministration of Metronidazole, Tetracycline, and Bismuth	Coadministration of Metronidazole, Tetracycline, and Bismuth With Tegoprazan
Metronidazole		
AUC_{0-6}, h • μg/mL	116.71 (22.47)	119.50 (17.51)
$C_{ss,max}$, μg/mL	23.37 (4.51)	24.99 (3.24)
$C_{ss,min}$, μg/mL	16.87 (3.68)	17.09 (3.08)
$C_{ss,av}$, μg/mL	19.45 (3.75)	19.92 (2.92)
$T_{ss,max}$, h	1.5 [0.5–2.0]	1.5 [0.75–4.0]
$t_{1/2}$, h	11.86 (2.52)	11.71 (2.78)
CL_{ss}/F, L/h	4.42 (0.80)	4.26 (0.58)
Tetracycline		
AUC_{0-6}, h • μg/mL	23.12 (3.70)	14.69 (3.33)
$C_{ss,max}$, μg/mL	4.78 (0.73)	3.13 (0.78)
$C_{ss,min}$, μg/mL	3.21 (0.61)	2.08 (0.46)
$C_{ss,av}$, μg/mL	3.85 (0.62)	2.45 (0.56)
$T_{ss,max}$, h	1.5 [1.0–1.5]	1.5 [1.0–2.0]
$t_{1/2}$, h	9.73 (1.25)	10.13 (1.87)
CL_{ss}/F, L/h	22.18 (3.86)	36.33 (11.65)
Bismuth		
AUC_{0-6}, h • ng/mL	48.57 (25.17)	70.77 (26.04)
$C_{ss,max}$, ng/mL	23.02 (15.84)	27.86 (13.72)
$C_{ss,min}$, ng/mL	4.04 (1.70)	6.25 (2.10)
$C_{ss,av}$, ng/mL	8.09 (4.20)	11.79 (4.34)
$T_{ss,max}$, h	0.75 [0.5–1.0]	0.88 [0.5–1.5]
$t_{1/2}$, h	24.27 (16.40)	17.71 (5.26)
CL_{ss}/F, L/h	6422.94 (3444.95)	3905.32 (1618.09)

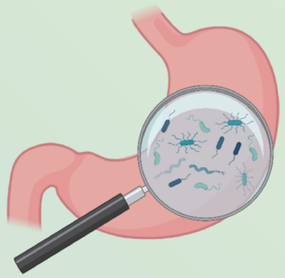
Ji-Young Jeon, et al. Clinical Therapeutics 2021;43(4)

Tegoprazan

Ten-day tegoprazan-based concomitant therapy as a first-line treatment for *Helicobacter pylori* eradication

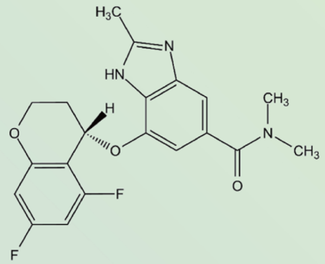
Prospective, single-arm, single-center, primitive study

Patients



84 participants of *Helicobacter pylori*

Methods



Tegoprazan-based, nonbismuth-containing quadruple therapy
(tegoprazan, amoxicillin, clarithromycin, metronidazole)

Results

	Intention-to-treat	*Per-protocol*
All patients	**90.5%** (95% CI 82.1-95.8)	**96.2%** (95% CI 83.4-97.6)
Patients with antibiotics resistance	**66.1%**	

Conclusion

The 10-day tegoprazan-based concomitant therapy may be an effective first-line treatment for eradicating *H. pylori.*

Kwon YH, et al. Korean Journal of Internal Medicine 2023;38(4):493-503.

Tegoprazan

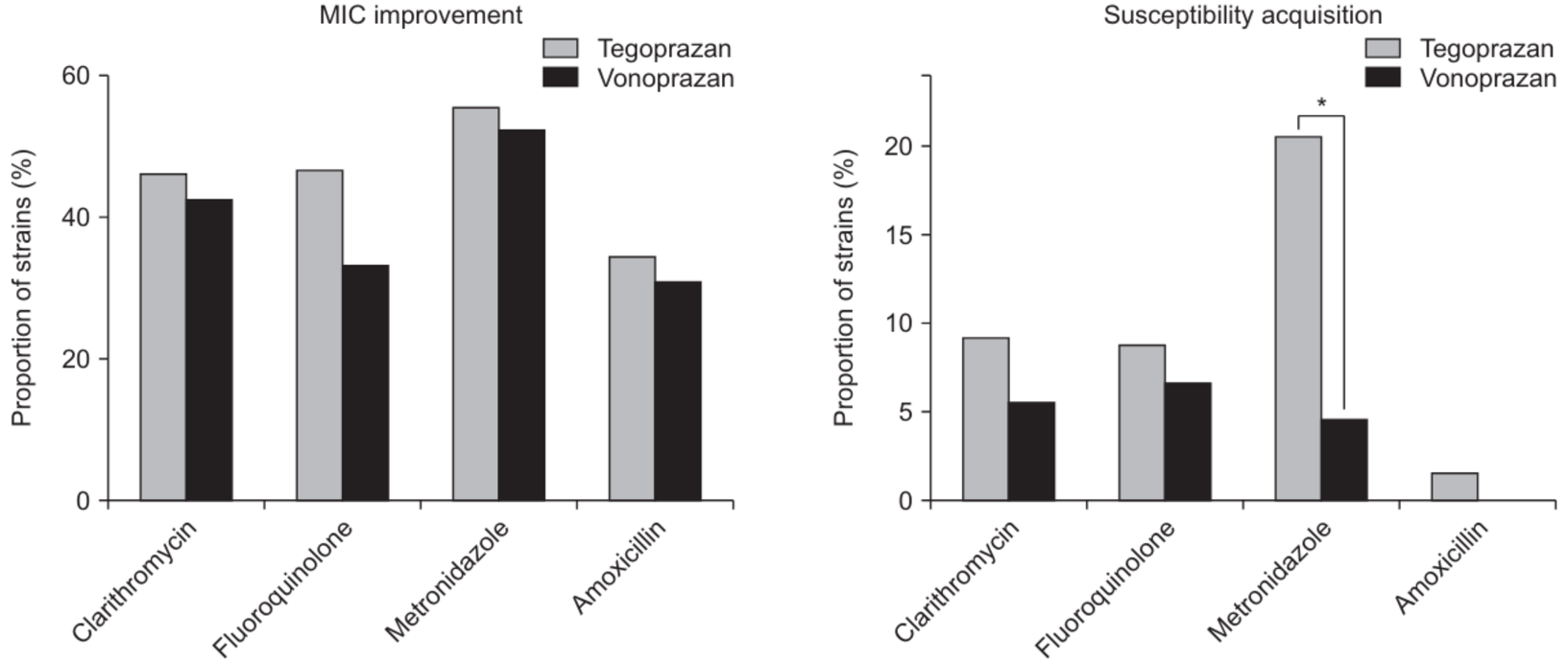
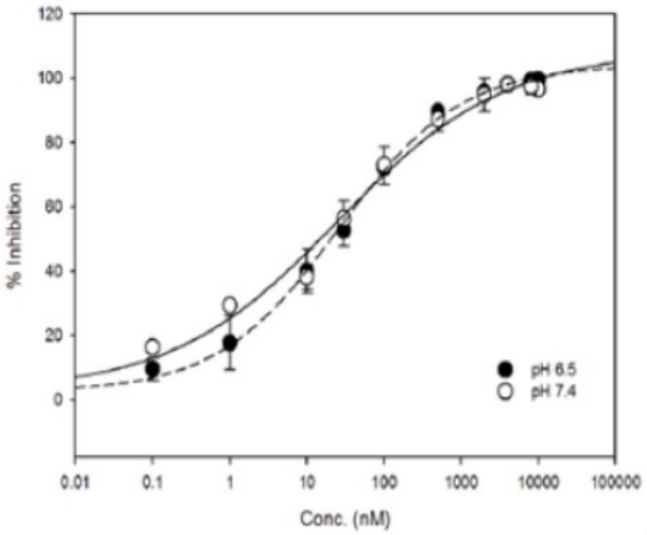


Fig. 3. Comparison of the improved susceptibility of *Helicobacter pylori* to vonoprazan and tegoprazan. (A) There was no difference in the minimum inhibitory concentration (MIC) between vonoprazan and tegoprazan. (B) Tegoprazan demonstrated more frequent susceptibility acquisition with metronidazole than with vonoprazan (20.6% vs 4.7%, p=0.014). *Statistically significant, p<0.05.

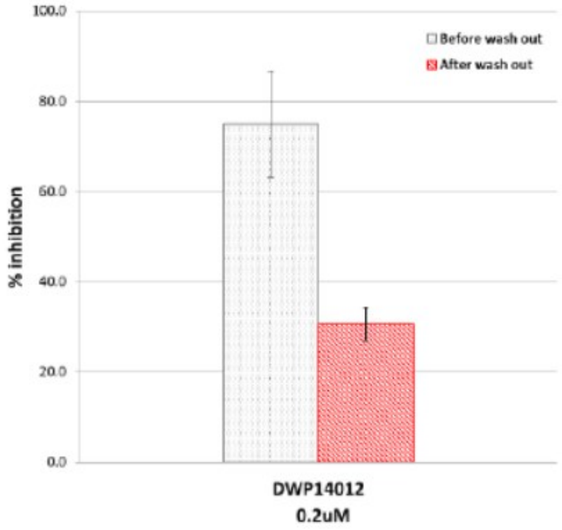
Lee JW, et al. Gut Liver 2020

Fexuprazan

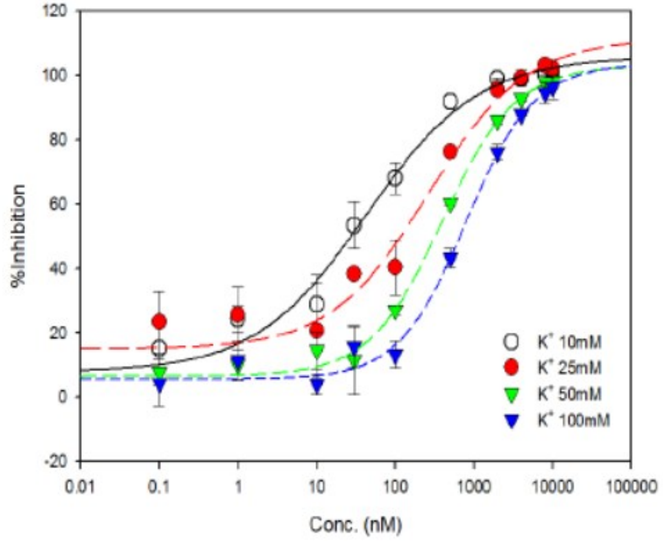
Fexuprazan is potent potassium competitive & reversible Acid Pump Antagonist (IC50: 25 nM).



(A) Inhibitory effect on H^+/K^+-ATPase activity



(B) Reversible mechanism of action



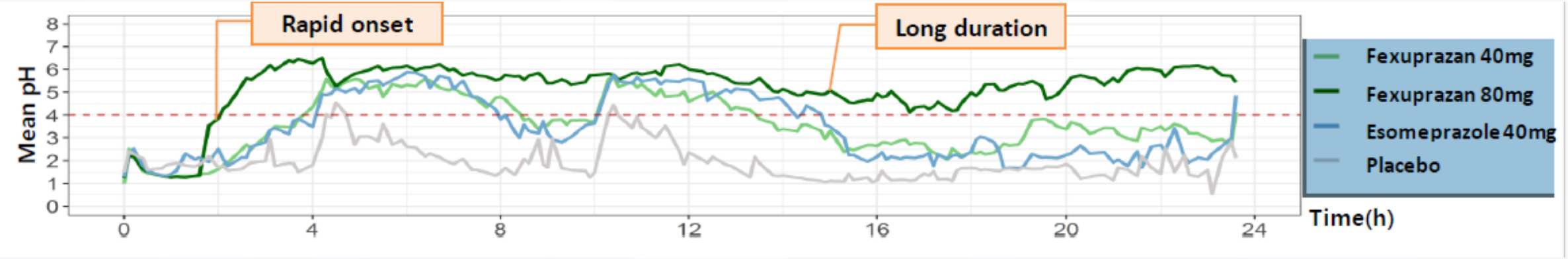
(C) K^+-competitive inhibition on H^+/K^+-ATPase

* IC_{50}: 25 nM (pH7.4) / 26 nM (pH6.5)

Pharmaceuticals (Basel). 2022 Jun; 15(6): 709

Fexuprazan

Fexuprazan demonstrated: rapid onset time and potent acid suppressive effect in humans, excellent safety and tolerability, favorable pharmacokinetic profiles.

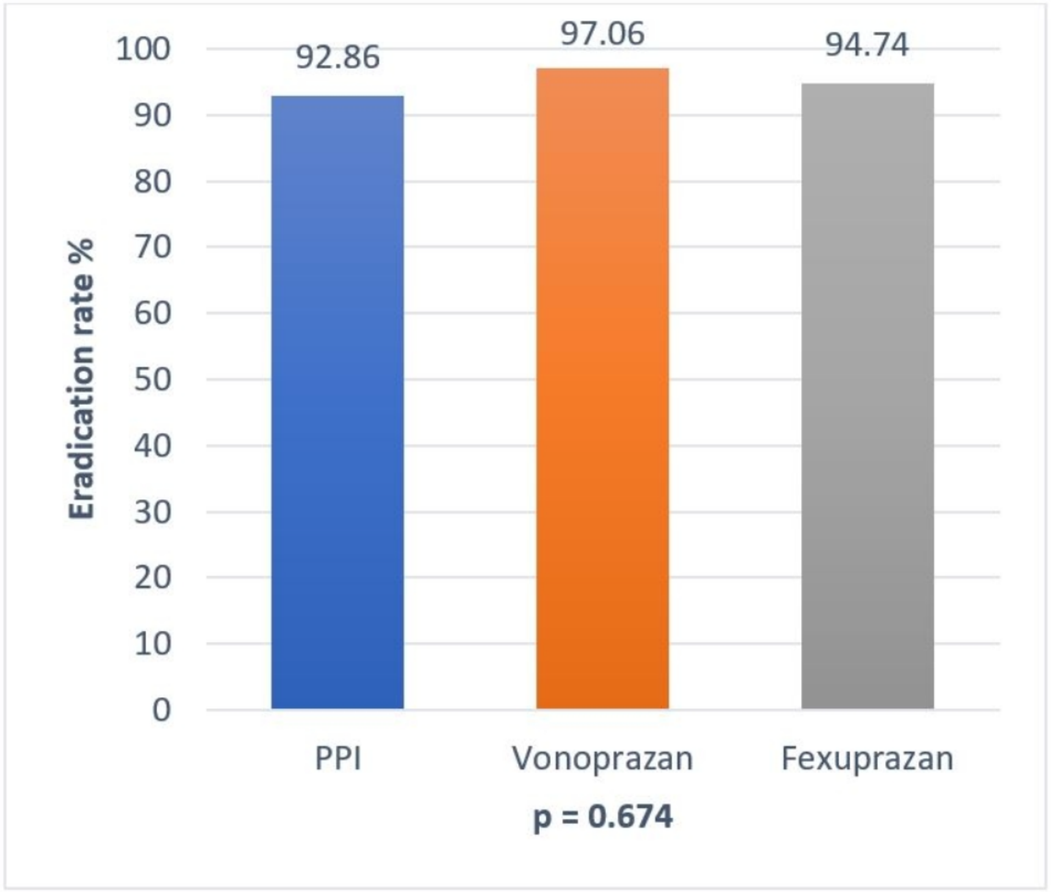


Pharmacodynamic properties demonstrated rapid (~2h) and sustained inhibition (24h pH holding time≥pH4 : 87.4%) of gastric acid secretion compared to esomeprazole in a dose dependent manner.

Pharmaceuticals (Basel). 2022 Jun; 15(6): 709

Fexuprazan

H. pylori eradication rates among the PPI, Vonoprazan and Fexuprazan-based regimens, determined 4 weeks post treatment, were not statistically different (p = 0.674).

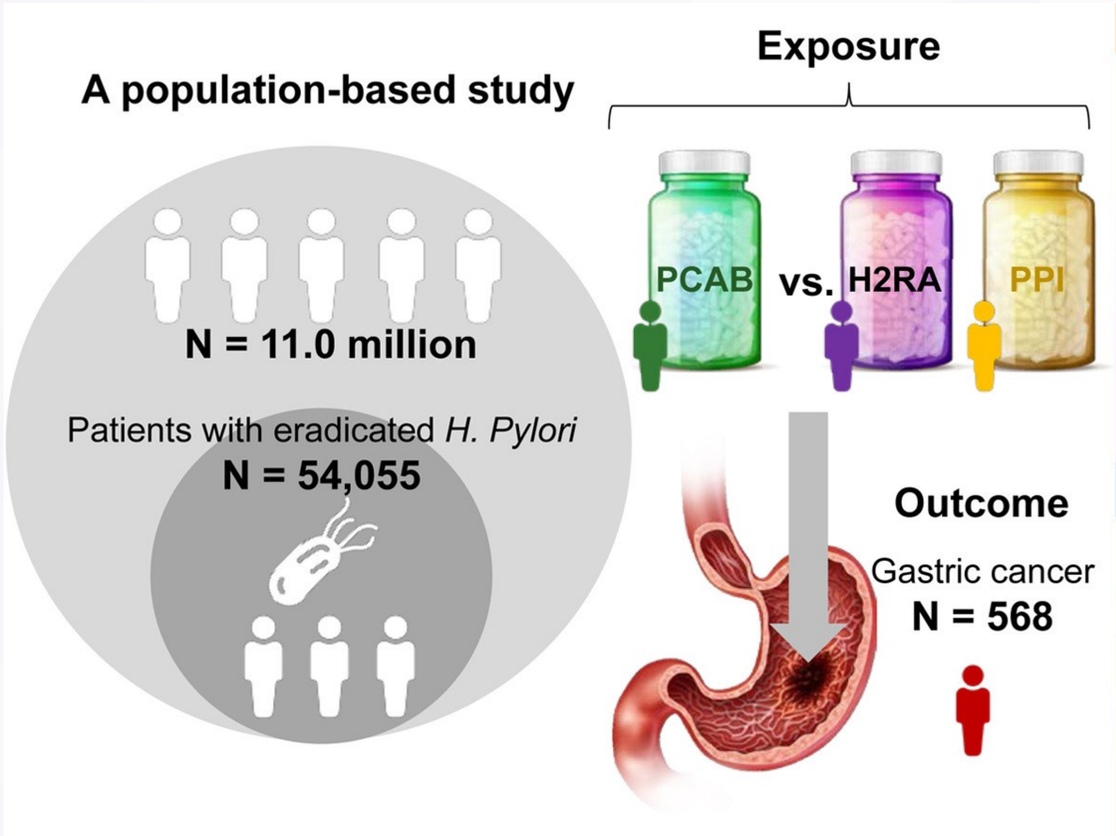


EFFICACY OF NOVEL POTASSIUM-COMPETITIVE ACID BLOCKERS, VONOPRAZAN AND FEXUPRAZAN, VERSUS CONVENTIONAL PROTON PUMP INHIBITOR-BASED TRIPLE THERAPY FOR ERADICATION OF *HELICOBACTER PYLORI*, A RETROSPECTIVE COHORT STUDY IN A PHILIPPINE TERTIARY HOSPITAL

Jose Maria Gonzalez
Author(s): Jose Maria I. Gonzalez, Jose Luis Matthias Z. Sollano, Miguel Edgardo Fores, Angelo Lozada

DDW ePoster Library. Gonzalez J. 05/18/2024; 414299; Sa1389

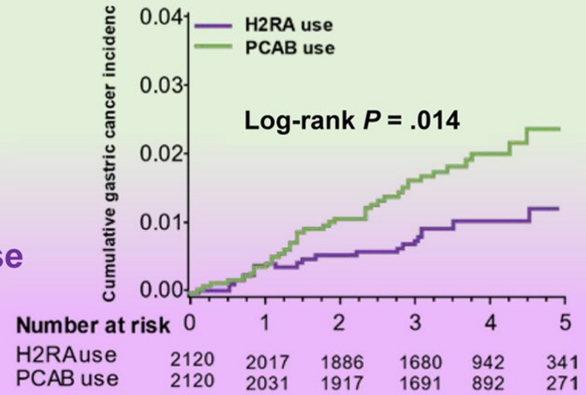
Asociación entre Vonoprazan y riesgo de cancer gástrico después de erradicación de *H. pylori*



Main analysis

PCAB users
vs
H2RA users

GC risk
PCAB use > H2RA use
Hazard Ratio: 1.92



Sensitivity analysis

PCAB users
vs
PPI users

GC risk
PCAB use ≒ PPI use
Hazard Ratio: 0.88

Duration/Dose Dependency

GC risk
PCAB use > 3 years
Hazard Ratio: 2.36

PCAB high-dose use
Hazard Ratio: 3.01

Clinical Gastroenterology and Hepatology

Arai J, et al. Clin Gastroenterol Hepatol 2024;22:P1217-1225.

¡Muchas gracias!

CURSO DE AVANCES EN GASTROENTEROLOGÍA
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