Novel Acid Blocker in *H. pylori* Eradication

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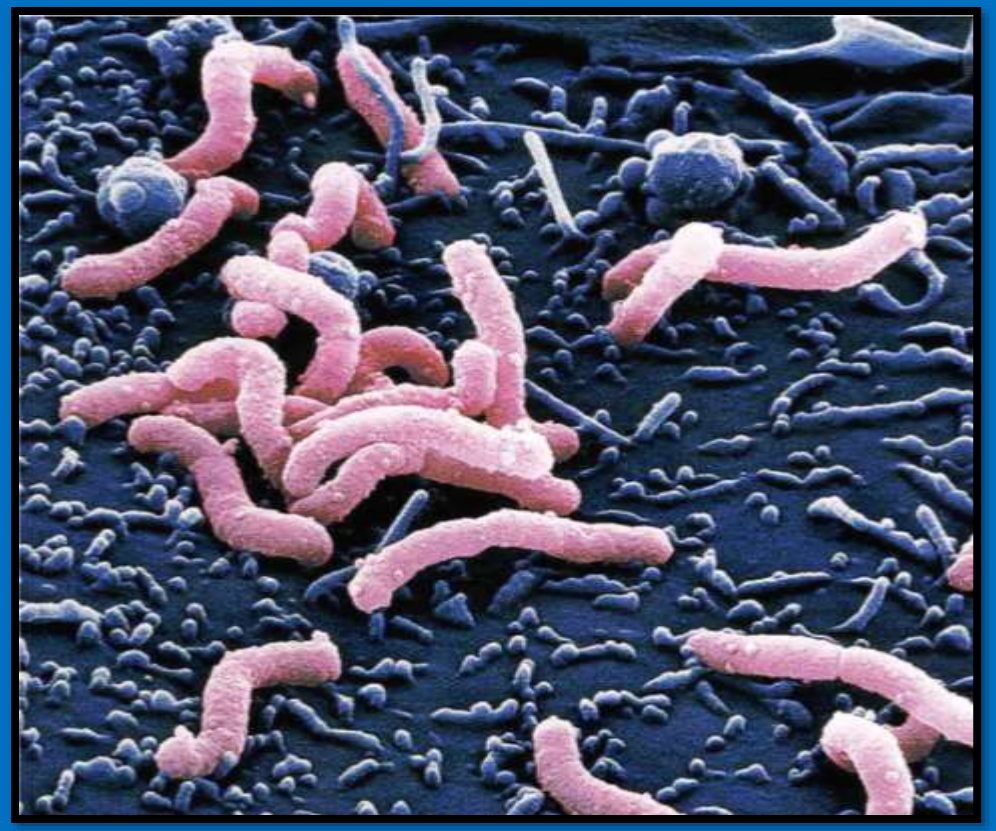
10th August 2025

Contents

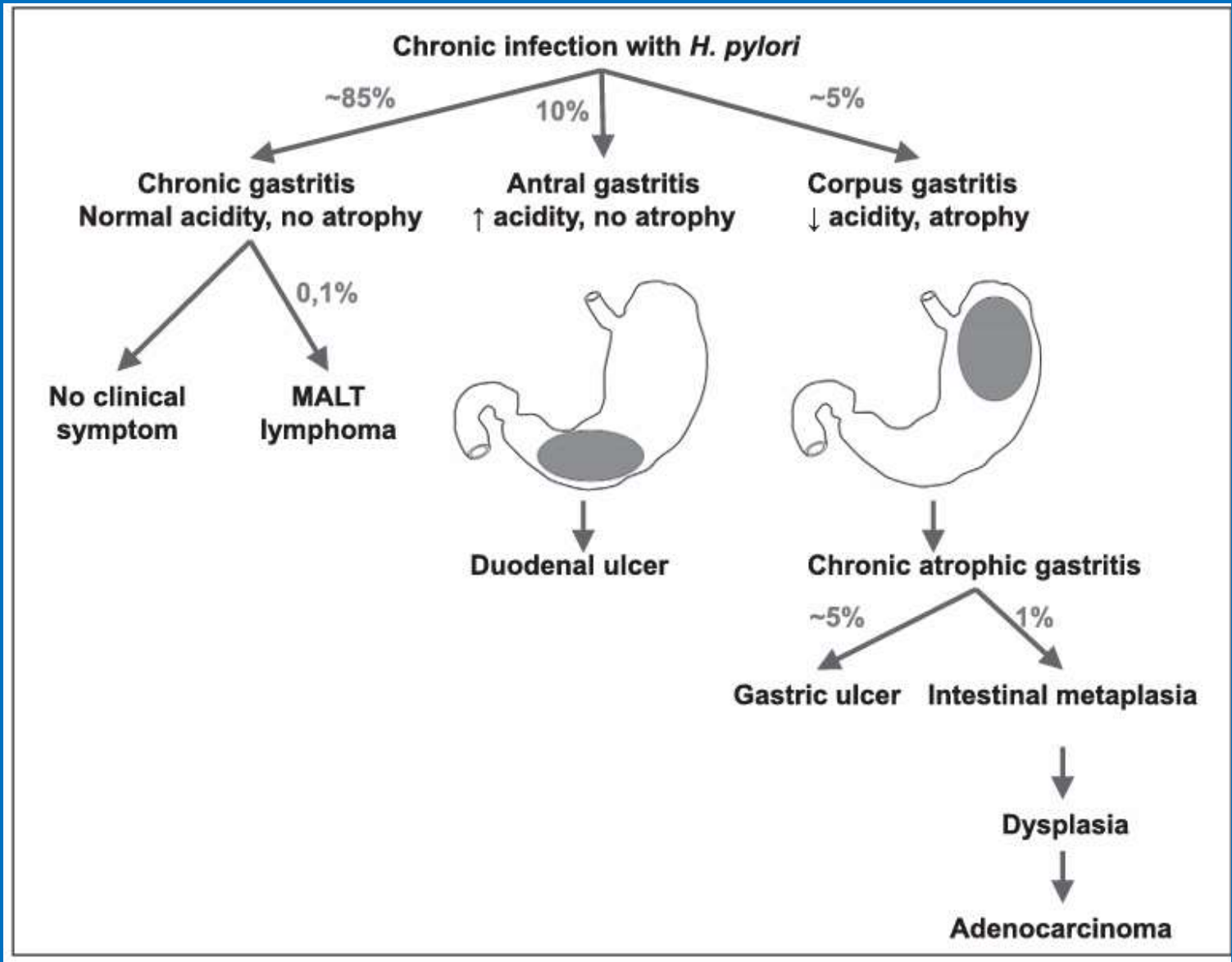
- Global burden of H. pylori infection
- Current practice of H. pylori eradication
- Changing concept of H. pylori eradication in the era of Novel Acid Blocker
- Role of Novel Acid Blocker in H. pylori eradication

Global burden of H. pylori infection

- Over half of the world's population is infected with H. pylori
- The most prevalent bacterial infection in human
- Unless treated, usually persists lifelong infection
- First recognized bacterial carcinogen
- Classified as class I carcinogen by World Health Organization since 1994



Consequences of H. pylori infection



Clin Microbiol Infect 2015; 21: 984–990

Correa cascade

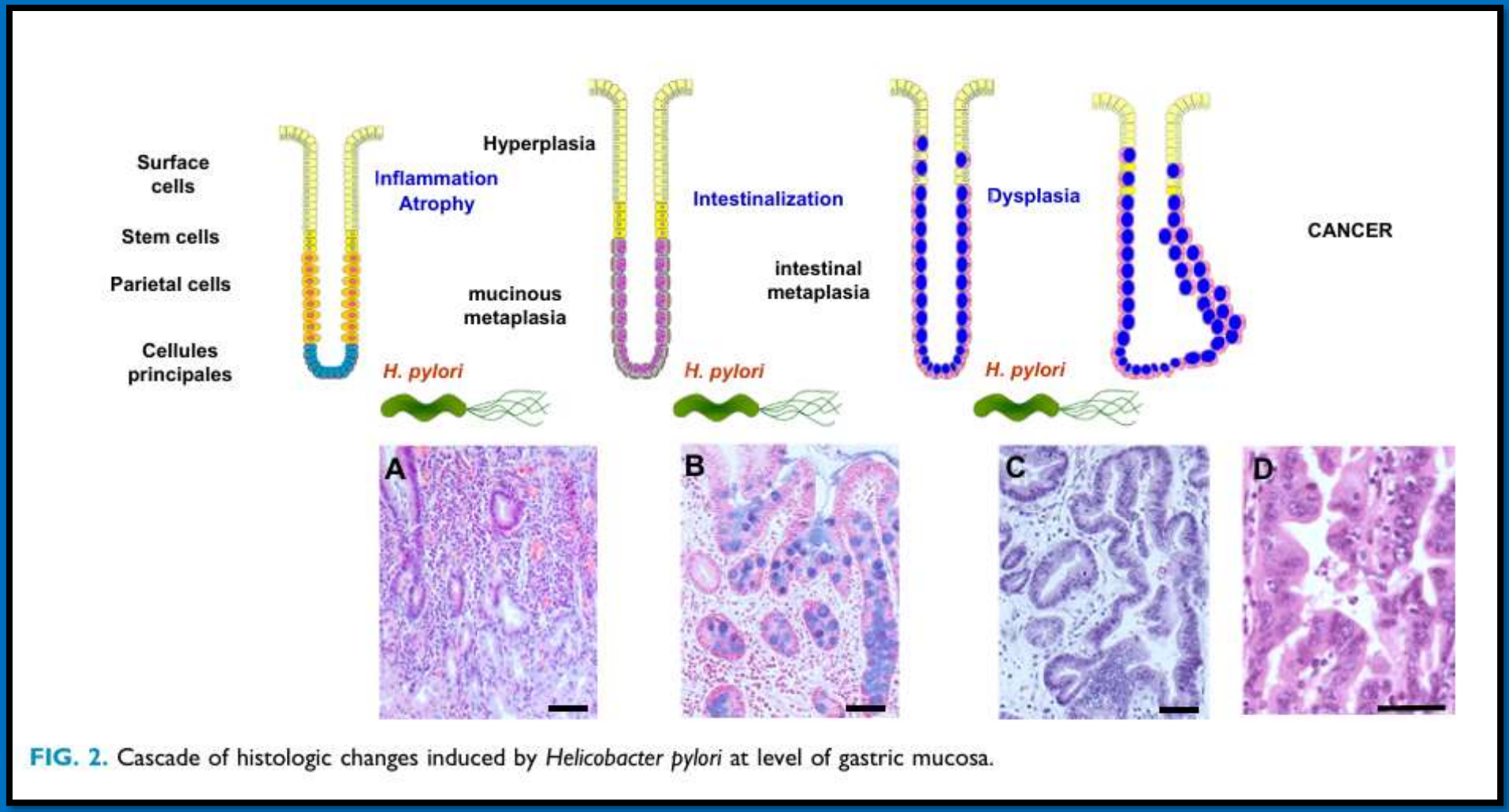
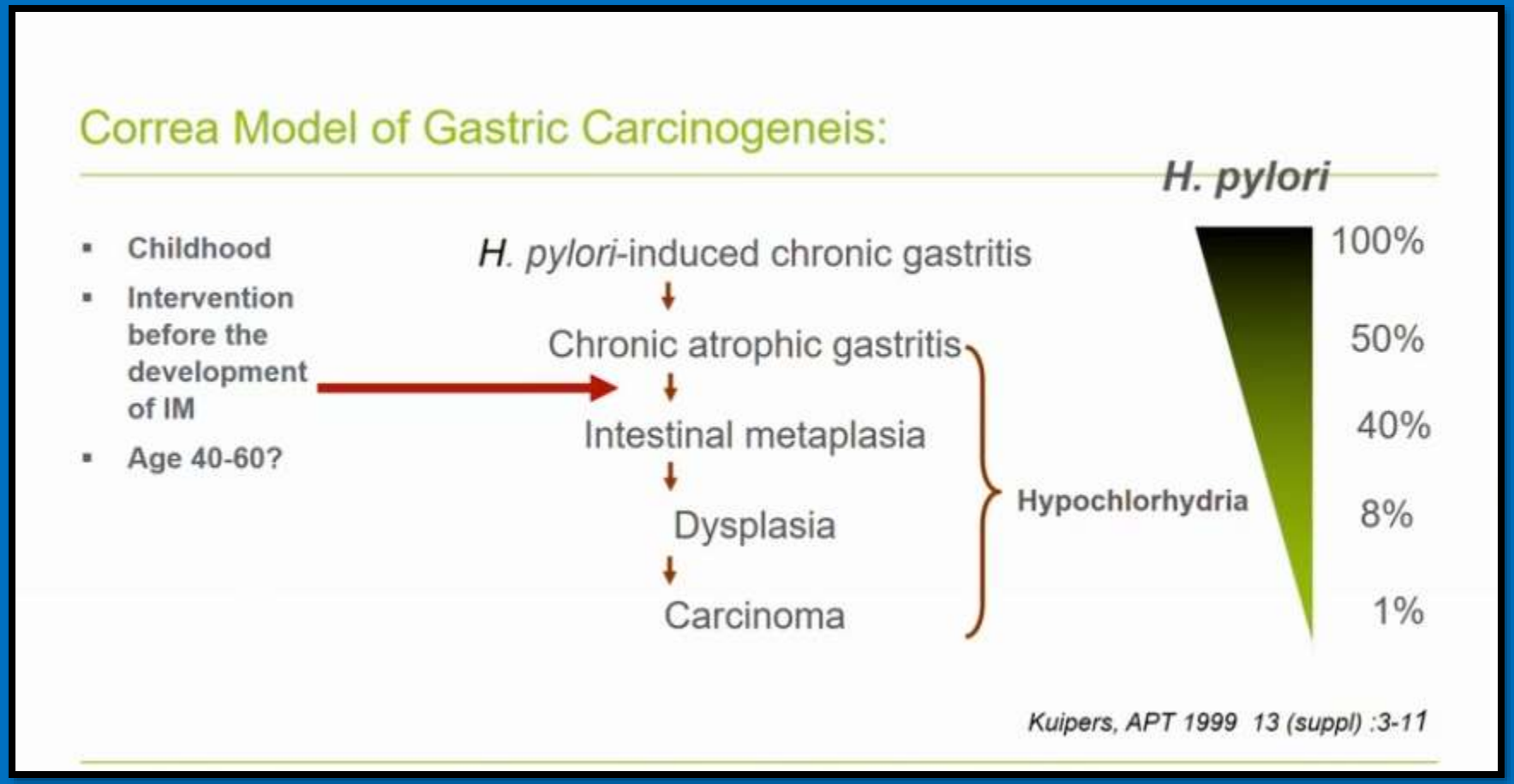


FIG. 2. Cascade of histologic changes induced by *Helicobacter pylori* at level of gastric mucosa.

Clin Microbiol Infect 2015; 21: 984–990

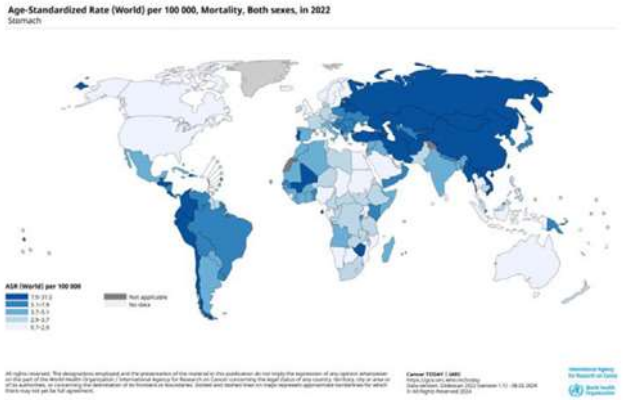
H. Pylori eradication

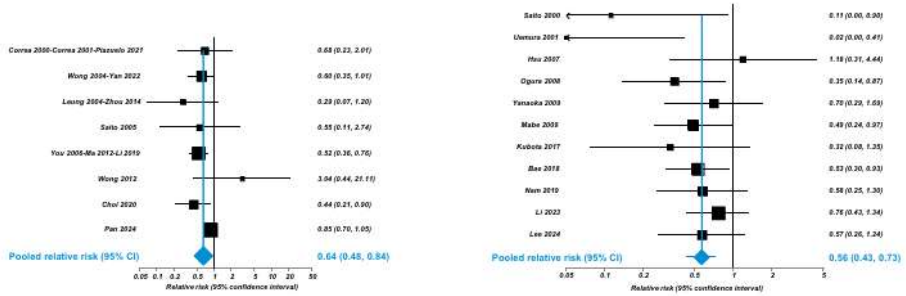
Prevent progression of chronic active gastritis to IM, dysplasia and gastric cancer



Eradication Therapy to Prevent Gastric Cancer in *Helicobacter pylori*-Positive Individuals: Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies

Gastric cancer is the fifth commonest cause of cancer death worldwide and is causally related to *Helicobacter pylori*.





In a meta-analysis of 8 randomized placebo-controlled trials of eradication therapy in 58,628 healthy *Helicobacter pylori*-positive adults, eradication therapy reduced future incidence of gastric cancer (above left figure). This effect was mirrored in 11 cohort studies containing 89,774 infected individuals with *Helicobacter pylori* (above right figure).

Gastroenterology

Gastroenterology 2025;169:261–276

- A meta-analysis suggests that *H. pylori* eradication lowers gastric cancer incidence by about 40%
- Early eradication of H. pylori is crucial, especially before the development of advanced changes like atrophic gastritis or intestinal metaplasia.

Current practice of *H. pylori* eradication

Current practice of *H. pylori* eradication

Triple therapy

Regimen	Drugs (doses)	Frequency	Duration (days)
PAC	PPI (SD) + Clarithromycin (500 mg) + Amoxicillin (1G)	BD	7 - 14
PCM	PPI (SD) + Clarithromycin (500 mg) + Metro (500 mg TDS)	BD	7 - 14

- No longer used as first line treatment in H. pylori eradication
- Increasing resistance to clarithromycin and metronidazole worldwide

H. Pylori Antibiotic resistance

H. pylori Antibiotic Resistance Rates in the US

a

Antibiotic(s)	% Resistant (N=2669 strains)
Clarithromycin	31.5
Levofloxacin	37.6
Metronidazole	42.1
Tetracycline	0.9
Amoxicillin	2.6
Rifabutin	0.2
Dual Metronidazole /Clarithromycin	11.7

Antibiotic susceptibility testing performed on 2669 strains from the US between 2011-2021

Ho J et al, Am J Gastroenterol 2022;117:1221

b

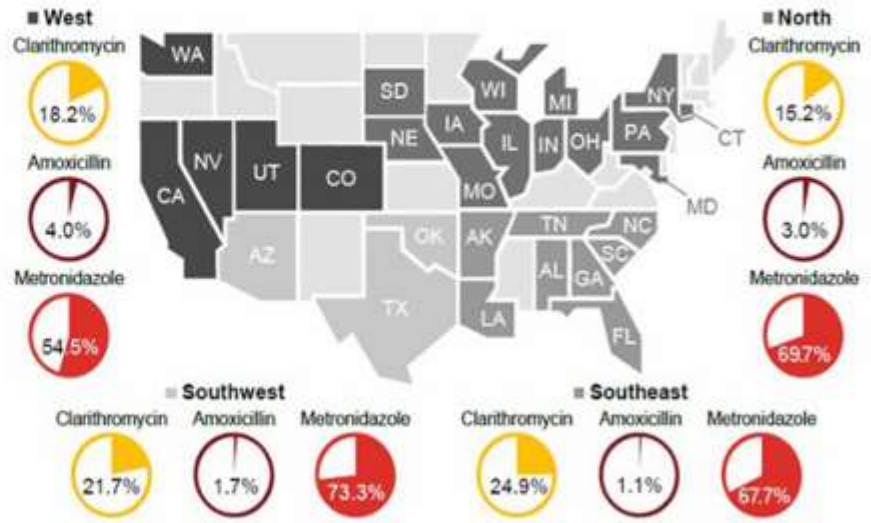
Overall resistance rates:

Clarithromycin **22.2%**

Amoxicillin **1.2%**

Metronidazole **69.2%**

US resistance rates by subregion:

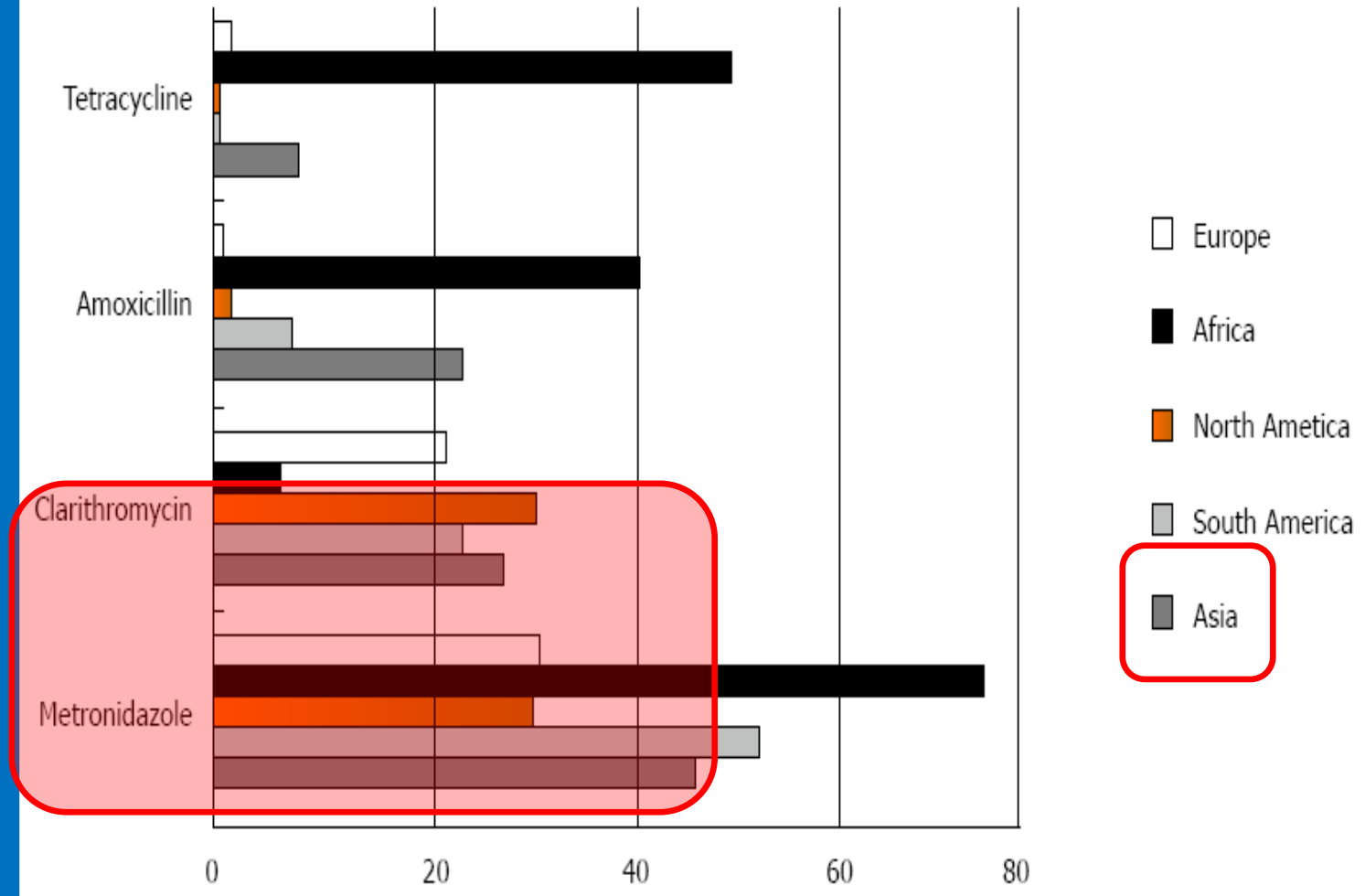


381 patients with *H. pylori* from the US underwent antibiotic sensitivity testing between 12/2019-1/2021

Megraud et al. Am J Gastroenterol 2023;118:269–275

- Increasing resistance of *H. pylori* to Clarithromycin, Metronidazole and Quinolones global concern
- Resistance to Amoxycillin, Tetracycline and Rifabutin is still rare.

Antimicrobial Resistance: Global Challanges



Antibiotic resistance rates to 4 most common used antibiotics in different continental areas

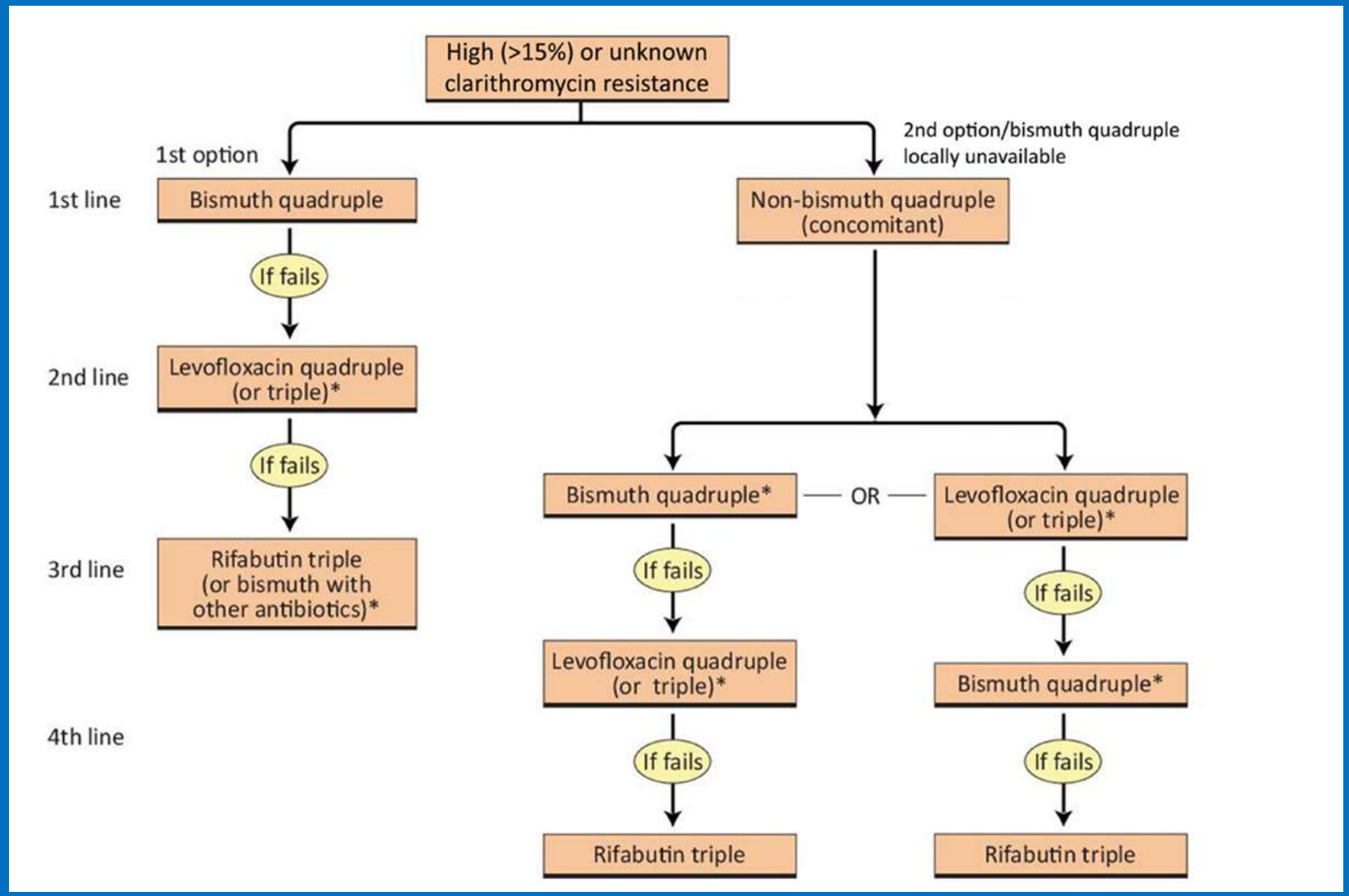
Ghotaslou R et al. *World J Methodol* 2015 September 26; 5(3)

Current practice of *H. pylori* eradication

- Empirical therapy
  - without knowledge of H. pylori's antibiotic resistance profile
- Susceptibility-guided therapy
  - based on knowledge of the antibiotic susceptibility test (AST)
    - culture-based
    - molecular

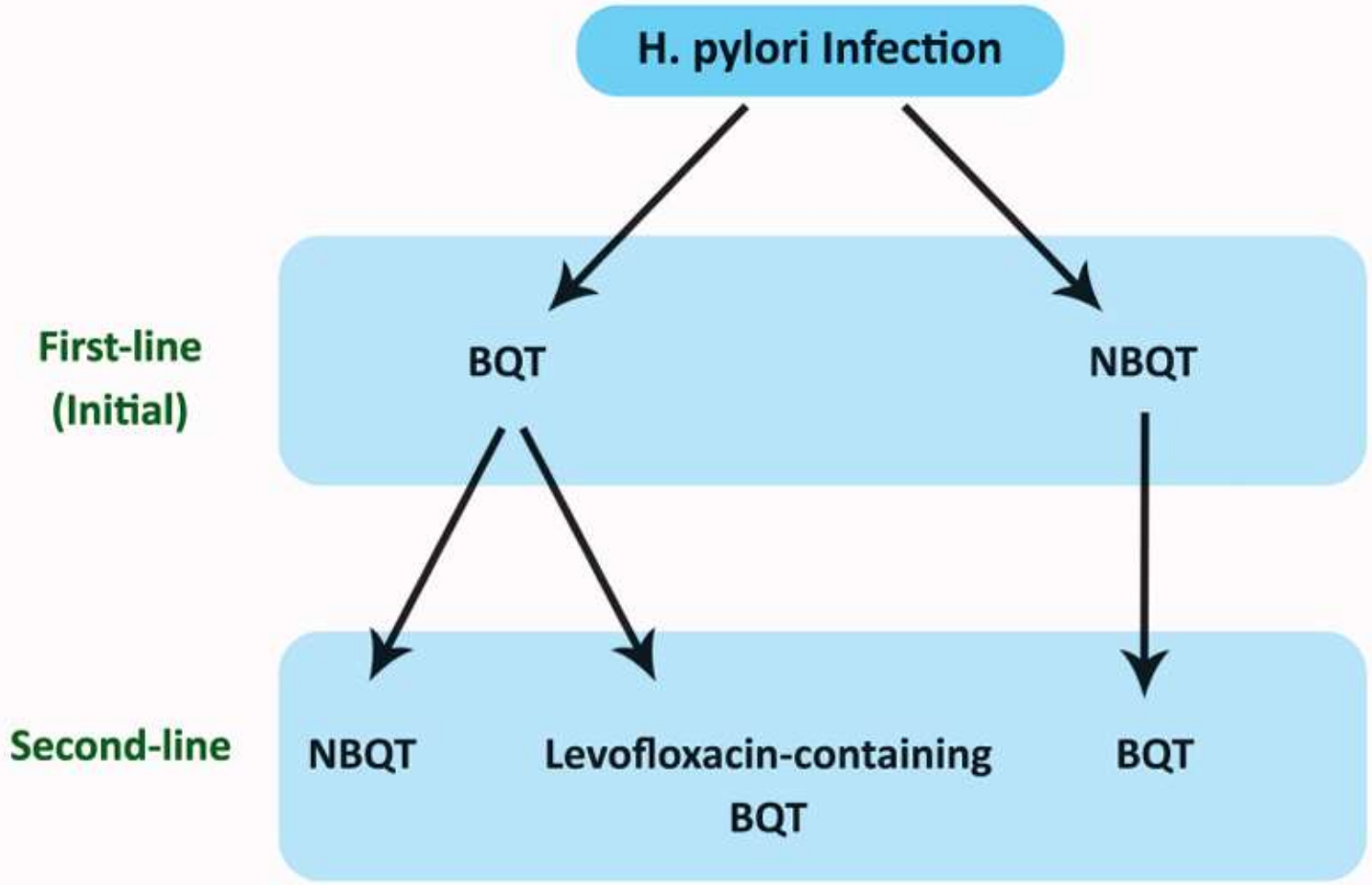
Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report

Peter Malfertheiner [1,2] Francis Megraud [3] Theodore Rokkas [4,5]
Javier P Gisbert [6,7] Jyh-Ming Liou [8] Christian Schulz [1,9]



Malfertheiner P, et al. Gut 2022;71:1724–1762.

Management of *Helicobacter Pylori* Infection
2024 Myanmar Consensus Report



Management of *Helicobacter Pylori* Infection
2024 Myanmar Consensus Report

First-Line (Initial) Therapy

Non-bismuth Quadruple Therapy (Concomitant Quadruple Therapy)	**Dosage**	**Duration**
Amoxicillin	1 g BID	14 days
Clarithromycin	500 mg BID	14 days
Tinidazole/Metronidazole*	500 mg BID	14 days
PPI	BID	14 days

Bismuth Quadruple Therapy	**Dosage**	**Duration**
Bismuth Subsalicylate	524 mg QID	14 days
Tetracycline	500 mg QID	14 days
Metronidazole*	500 mg TID	14 days
PPI	BID	14 days

Management of *Helicobacter Pylori* Infection 2024 Myanmar Consensus Report

Second-line therapy

Levofloxacin-Containing Bismuth Quadruple Therapy	Dosage	Duration
Levofloxacin	500 mg OD	14 days
Bismuth subsalicylate	524 mg QID	14 days
Amoxicillin	1 g BID	14 days
PPI	BID	14 days

Quadruple therapies

Regimen	Drugs (doses)	Frequency	Duration (days)
Non-bismuth quadruple (Concomitant)	PPI (SD) Amoxicillin (1G) Clarithromycin (500 mg) Nitroimidazole (500 mg)	BD	14

- Simple dosing frequency (BD)
- Better compliance
- Similar efficacy as BQT if local CLA resistance rate <15%
- If AST (Antibiotic Susceptibility Test) is available, prior testing before starting treatment (optional)

Quadruple therapies

Regimen	Drugs (doses)	Frequency	Duration (days)
Bismuth quadruple therapy	PPI (SD)	BD	14
	Bismuth subsalicylate (300 - 524mg)* Tetracycline (500 mg)	QID	
	Metronidazole (500 mg)	TDS	

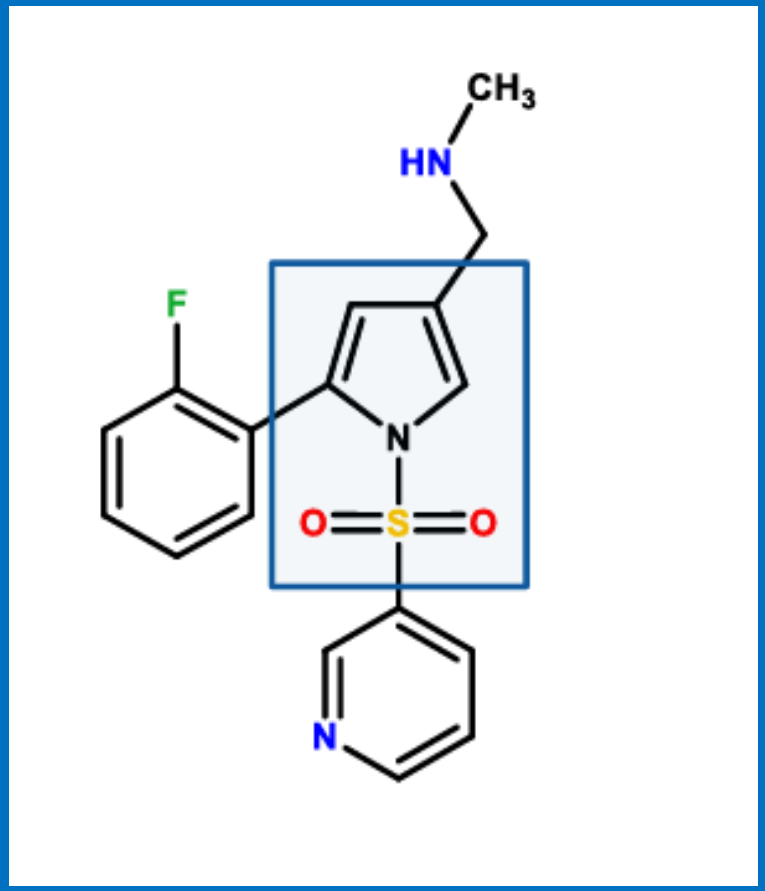
- Can be used in Penicillin allergy
- Not effected by CLA resistance
- High eradication rate 90%, even in areas with high CLA and MET resistance

- Complexity in dosing frequency
- Pill burden
- Side effects & tolerability
- Compliance issue
- Limited availability in some areas

Changing concept of *H. pylori* eradication in the era of Novel Acid Blocker

Vonoprazan in *H. pylori* eradication

- First introduced in Japan since 2015



OPEN ACCESS

ORIGINAL ARTICLE

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

A total of 650 patients randomized to receive 7 days of:

Vonoprazan triple therapy	vonoprazan 20 mg BD	amoxicillin 750 mg	clarithromycin (200 or 400 mg) BD
Lansoprazole triple therapy	lansoprazole 30 mg BD	amoxicillin 750 mg	clarithromycin (200 or 400 mg) BD

Patients with first-line treatment failure

Vonoprazan triple therapy	vonoprazan 20 mg BD	amoxicillin 750 mg	Metronidazole 250 mg BD

Murakami K, et al. Gut 2016;65:1439–1446

OPEN ACCESS

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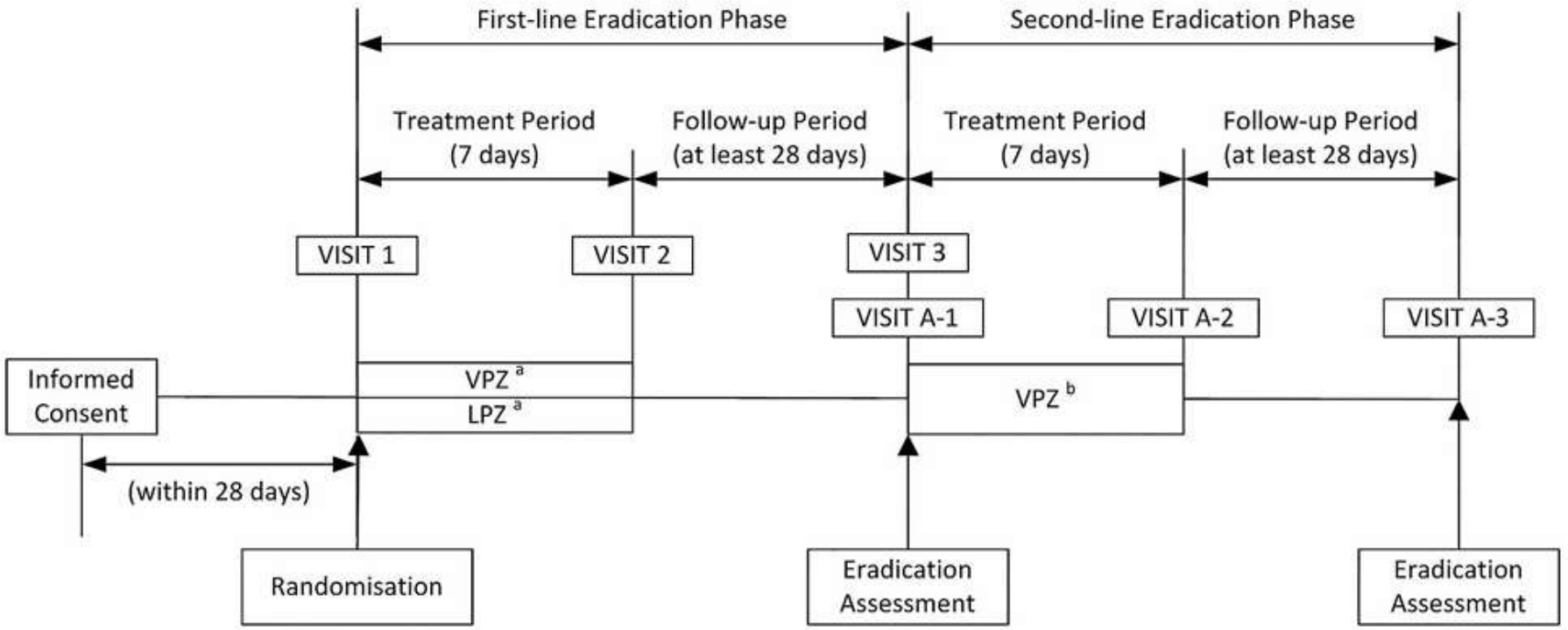
Vonoprazan, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for *Helicobacter pylori* eradication: a phase III, randomised, double-blind study



Murakami K, et al. Gut 2016;65:1439–1446

- Vonoprazan-based triple therapy demonstrated a non-inferior eradication rate of 93% compared to 76% for lansoprazole-based triple therapy

- *H. pylori* eradication rate in clarithromycin resistant strains was higher with vonoprazan-based triple therapy (82%) than with lansoprazole-based triple therapy (40%)

Murakami K, et al. Gut 2016;65:1439–1446

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ORIGINAL ARTICLE

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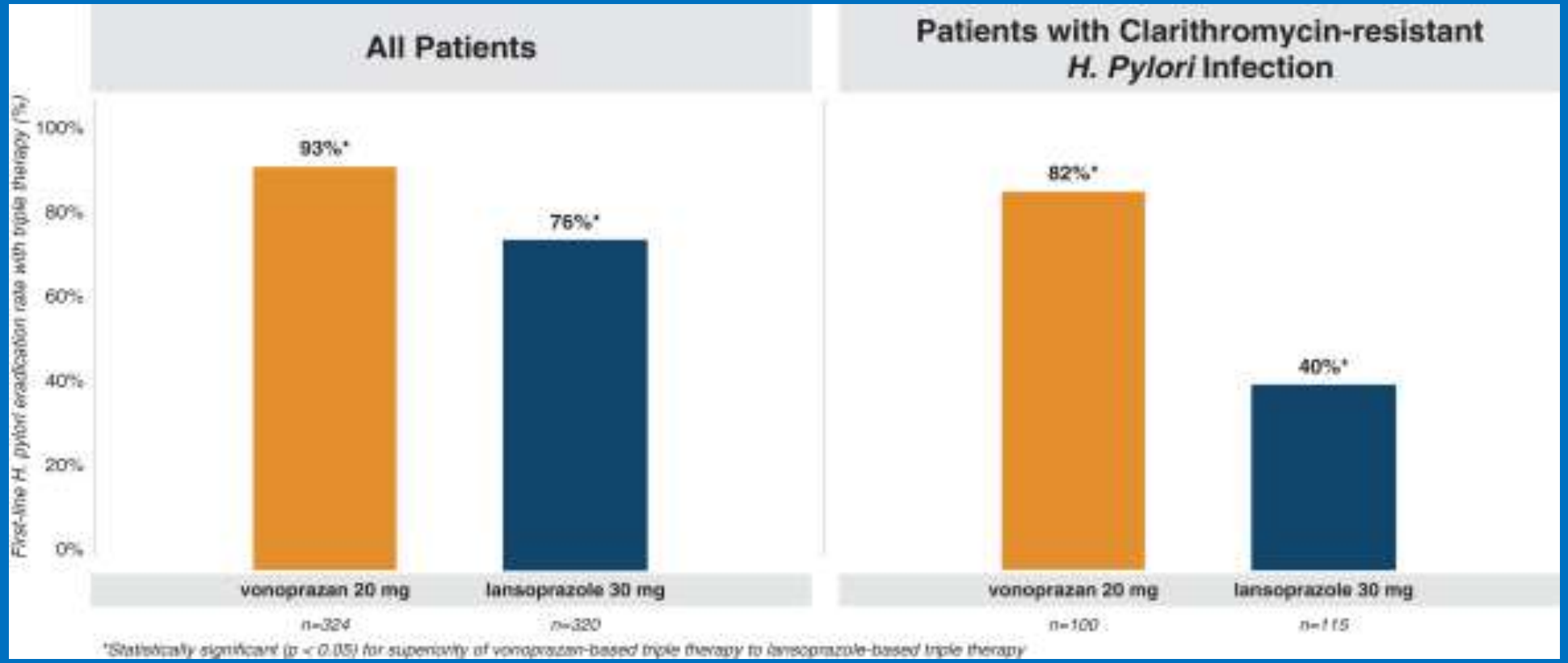
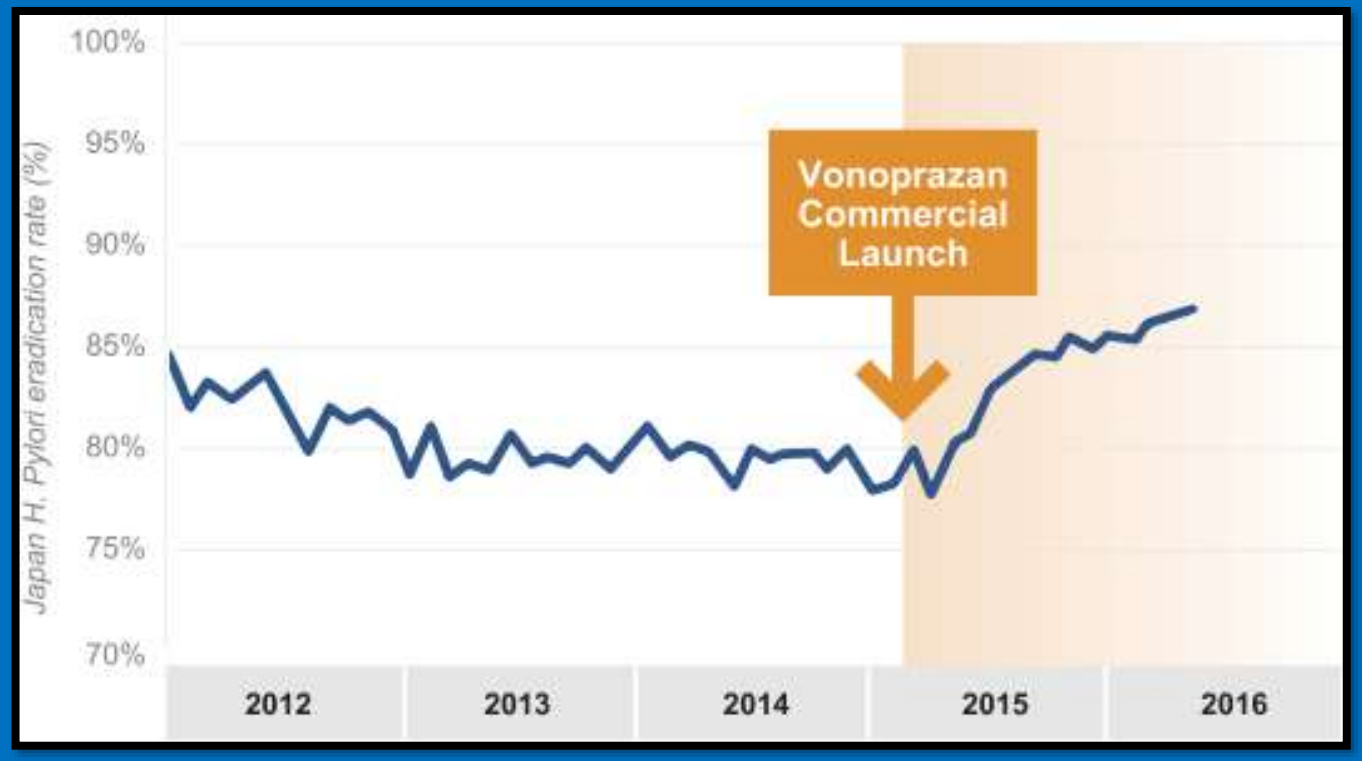


Murakami K, et al. Gut 2016;65:1439–1446

Eradication Rate of *H. pylori* Infection in Japan Before and After Launch of Vonoprazan



- Prior to vonoprazan's approval in late 2014, *H. pylori* eradication rate across Japan fell to below 80%
- Approximately one year after vonoprazan's launch, the eradication rate increased to greater than 85%.
- From January 2015 to March 2016, the eradication rate with PPI-containing regimens in Japan was between 78% and 82% while the eradication rate with vonoprazan-containing regimens was 91% across all claims in this analysis.

Digestion 2020;101:441–449 a

Vonoprazan Post-Marketing Safety in Japan

ADRs	Overall population
No. of patients evaluable for the safety analysis	550
Incidence of ADRs, *n* (%)	
Overall	17 (3.09)
Nervous system disorders	5 (0.91)
Dizziness	1 (0.18)
Dysgeusia	3 (0.55)
Hypogeusia	1 (0.18)
Gastrointestinal disorders	12 (2.18)
Abdominal discomfort	1 (0.18)
Abdominal distension	1 (0.18)
Constipation	1 (0.18)
Diarrhea	4 (0.73)
Feces hard	1 (0.18)
Nausea	4 (0.73)
Paresthesia oral	1 (0.18)
Feces soft	2 (0.36)
Skin and subcutaneous tissue disorders	5 (0.91)
Drug eruption	1 (0.18)
Eczema	1 (0.18)
Rash	2 (0.36)
Urticaria	1 (0.18)
General disorders and administration site conditions	1 (0.18)
Malaise	1 (0.18)

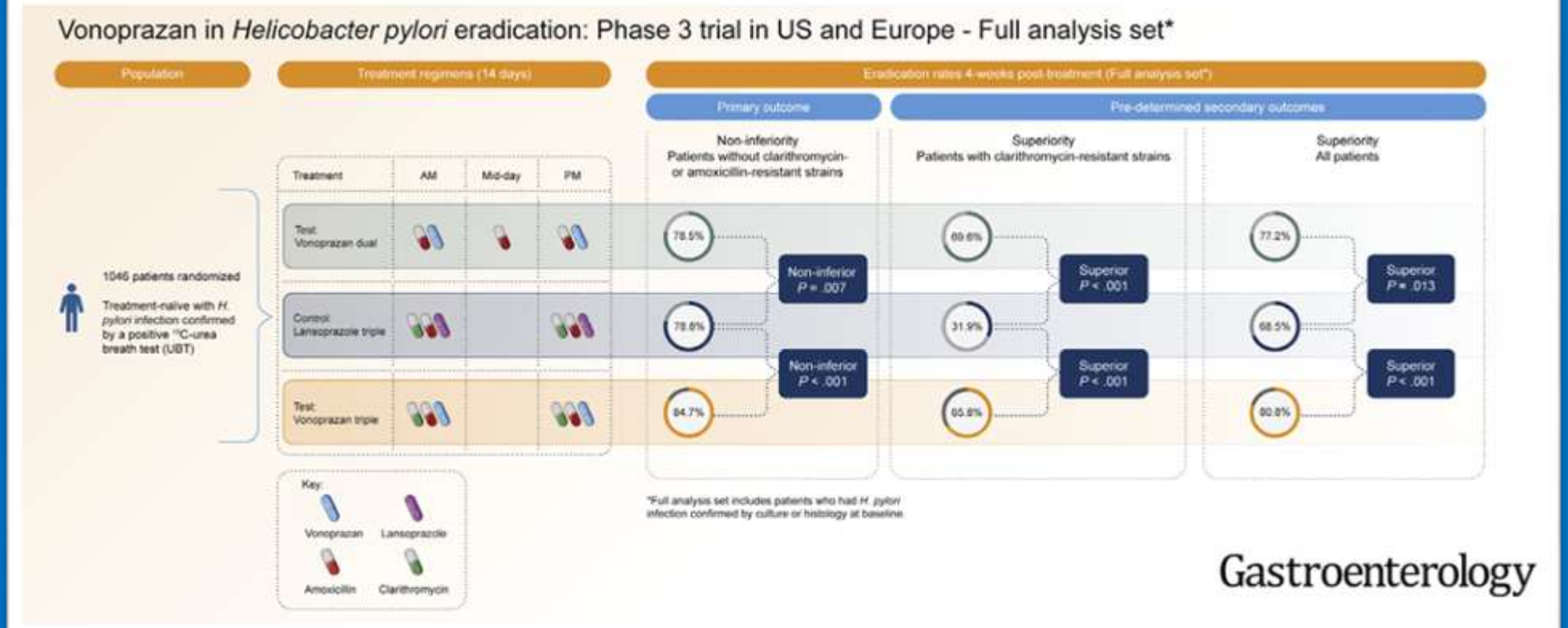
Expert Opinion on Drug Safety, 2019:18:12, 1255-1261

Gastroenterology 2022;163:608–619

HELICOBACTER PYLORI

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

William D. Chey,[1] Francis Mégraud,[2] Loren Laine,[3,4] Luis J. López,[5] Barbara J. Hunt,[6] and Colin W. Howden[7]



Gastroenterology 2022;163:608–619

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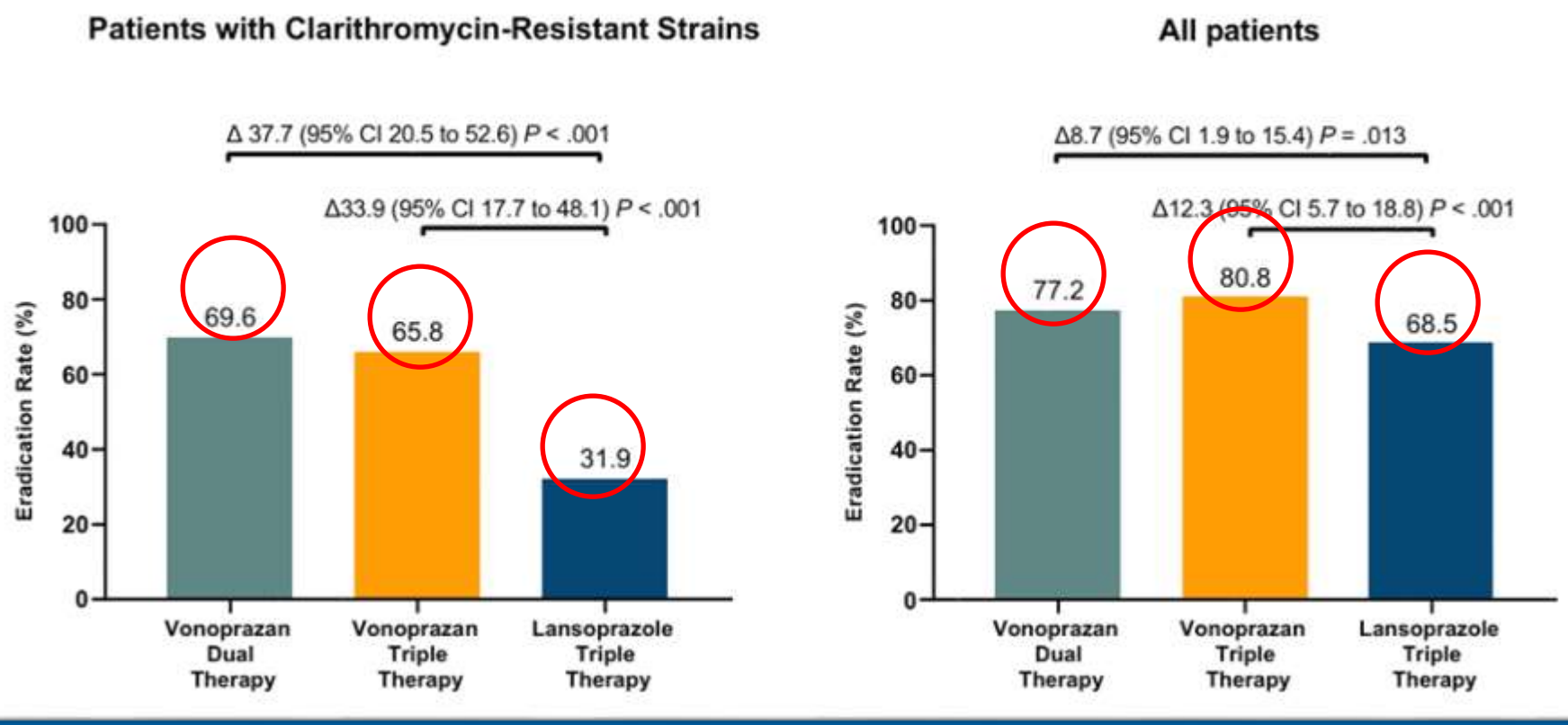

ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection

ACG Clinical Practice Guideline

Treatment of *H. pylori* Infection in North America

	Treatment Naïve	***Treatment-Experienced (Salvage)***		***Penicillin Allergy***
Regimen		Empiric	Proven antibiotic sensitivity	
Optimized Bismuth Quadruple	☑☑☑	☑☑	☑☑	☑☑☑ *
Rifabutin Triple	☑☑	☑☑	☑☑	
Vonoprazan Dual	☑☑	?	?	
Vonoprazan Triple			☑☑	
Levofloxacin Triple			☑☑	

☑☑☑ Recommended ☑☑ Suggested ? May be considered when other treatments are not options

Chey et al. *Am J Gastroenterol.* 2024. doi:10.14309/ajg.0000000000002968

All icons above are from Microsoft Powerpoint.

AJG The American Journal of GASTROENTEROLOGY

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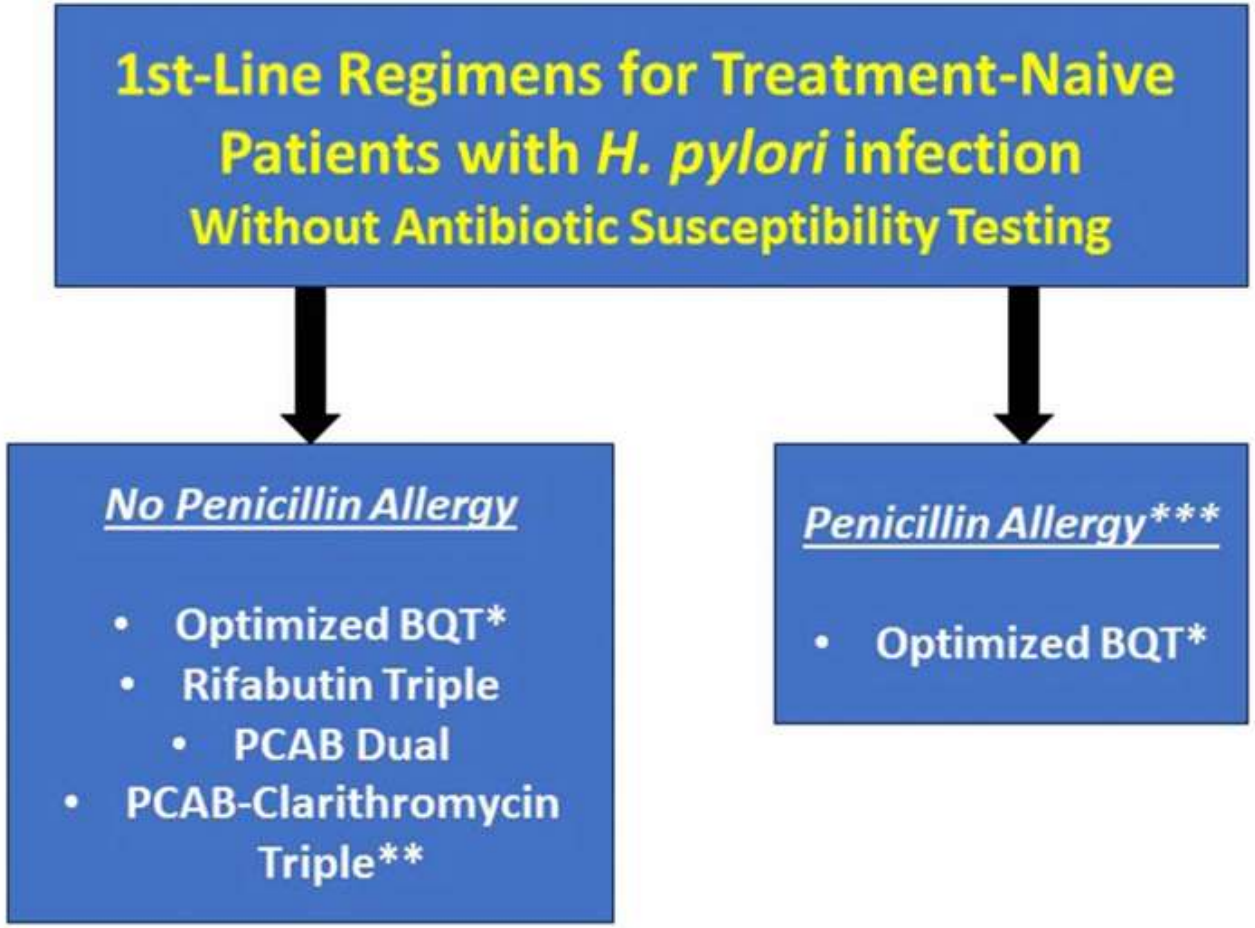


BQT, bismuth quadruple therapy, PCAB, potassium-competitive acid blocker

*Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline)

** Avoid in those with previous macrolide exposure

*** May require formal allergy testing

Chey et al. *Am J Gastroenterol.* 2024. doi:10.14309/ajg.0000000000002968

All icons above are from Microsoft Powerpoint.

AJG The American Journal of GASTROENTEROLOGY

Role of Novel Acid Blocker in H. pylori Eradication

Gastric Acid suppression in H. pylori Eradication

Gastric acid suppression enhances the effect of antibiotics in 2 ways

- Higher gastric pH increases the stability of the antibiotics.
- For example, amoxicillin and clarithromycin are chemically unstable at the low pH typically found in the human stomach.

Minimum inhibitory concentration of antibiotic required to eradicate 90% of *H. pylori in vitro*, or MIC_{90}

***H. pylori* MIC_{90} Values as a Function of pH**

	MIC_{90} (mg/L)		
	pH 7.5	pH 6.0	pH 5.5
Ampicillin	0.06	0.25	0.5
Clarithromycin	0.03	0.06	0.25

As pH increases, the amount of antibiotic required for 90% eradication decreases substantially.

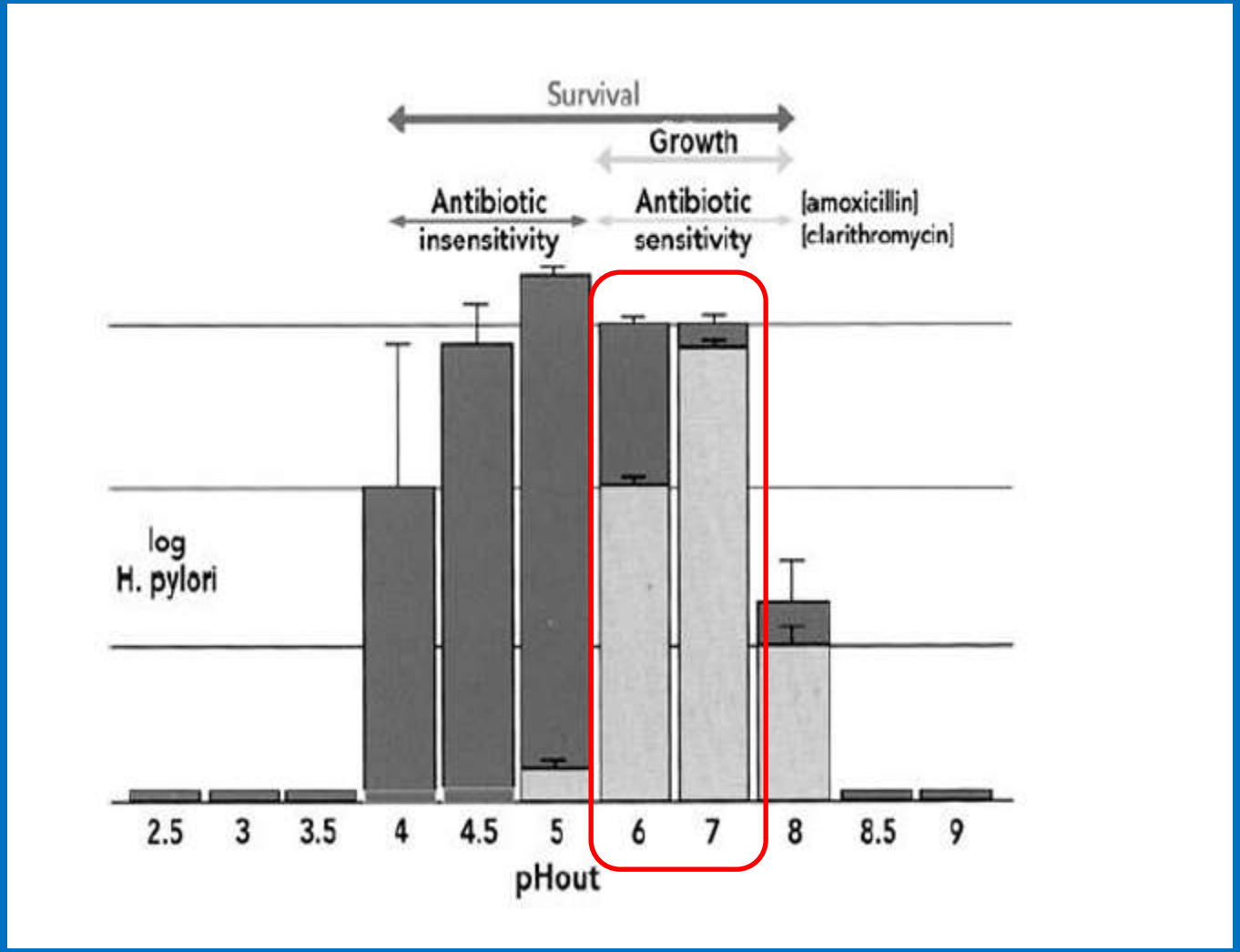
Gastric Acid suppression in H. pylori Eradication

Gastric acid suppression enhances the effect of antibiotics in 2 ways

- Higher gastric pH increases the stability of the antibiotics.
- For example, amoxicillin and clarithromycin are chemically unstable at the low pH typically found in the human stomach.

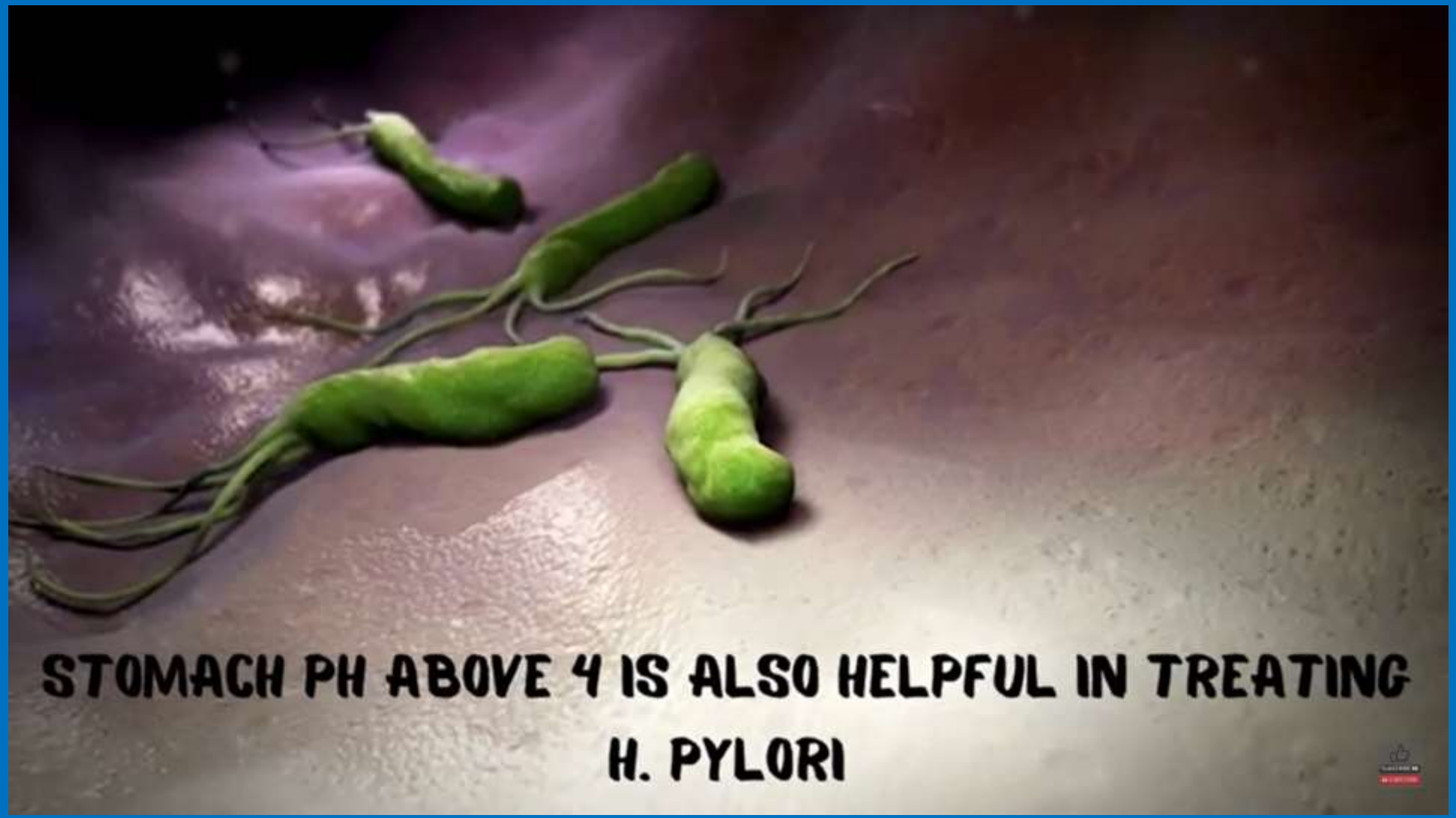
- Antibiotics, including amoxicillin and clarithromycin, are most potent against *H. pylori* at the time of maximum bacterial replication, which occurs at pH 6.0 to 7.0.
- *H. pylori* is in a dormant state at lower pH values, which reduces the effectiveness of the antibiotics.

Influence of pH variation on the antibiotic susceptibility of H. pylori

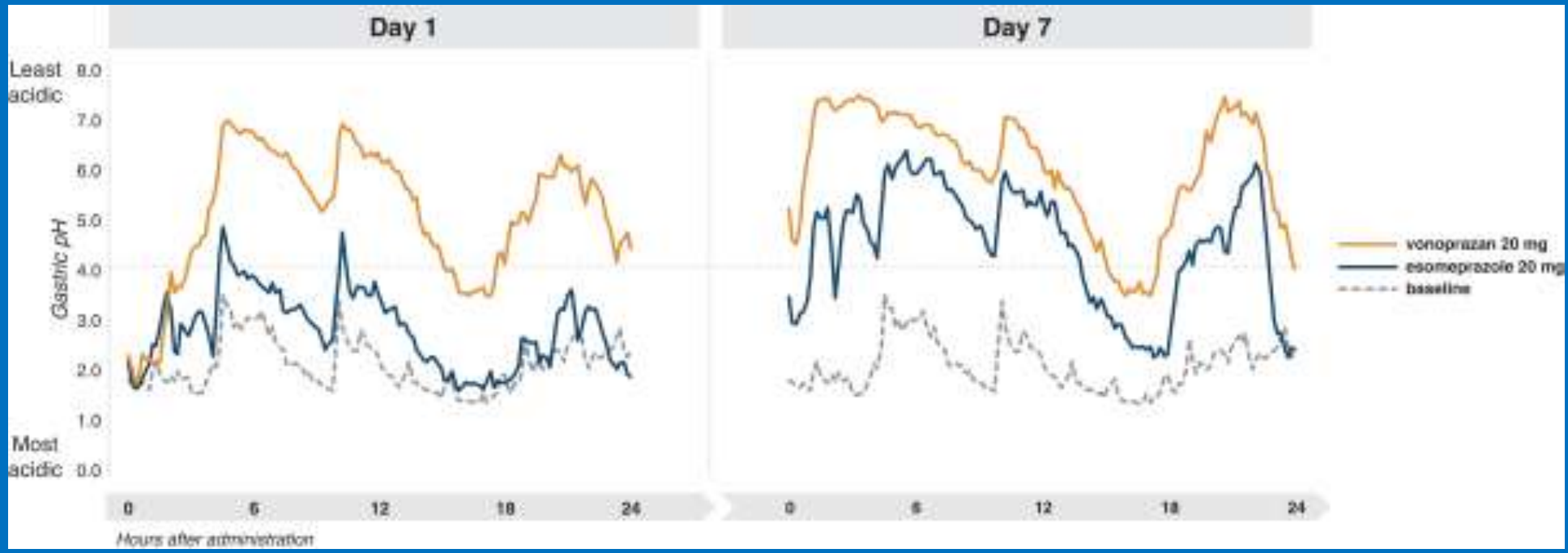


Graham DY, Fischbach L. Gut. 2010 - Volume 59 – 8

Helicobacter pylori treatment in the era of increasing antibiotic resistance

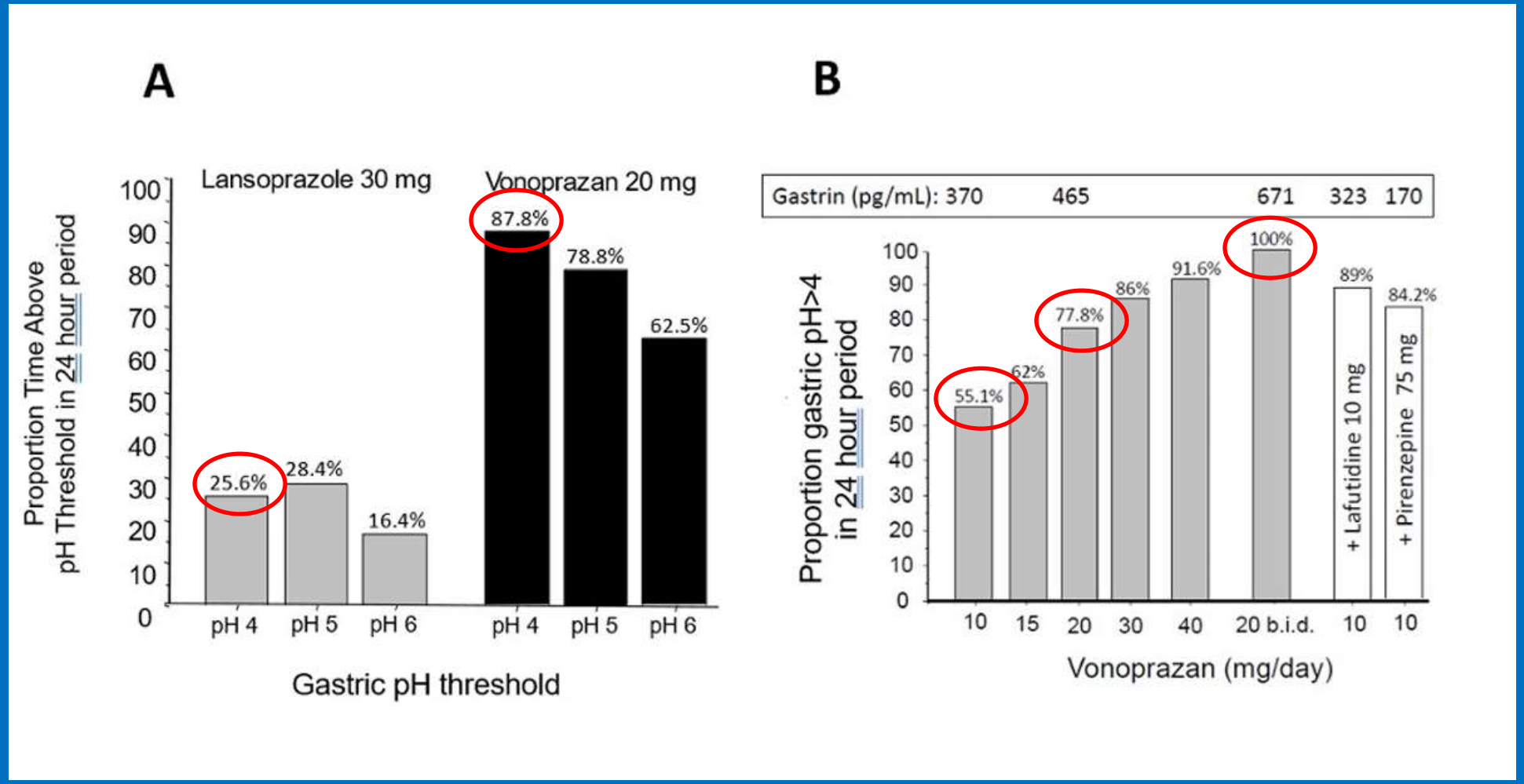

STOMACH PH ABOVE 4 IS ALSO HELPFUL IN TREATING
H. PYLORI

Improved Onset and Potency of pH Control of Vonoprazan vs. Esomeprazole at Day 1 and Day 7



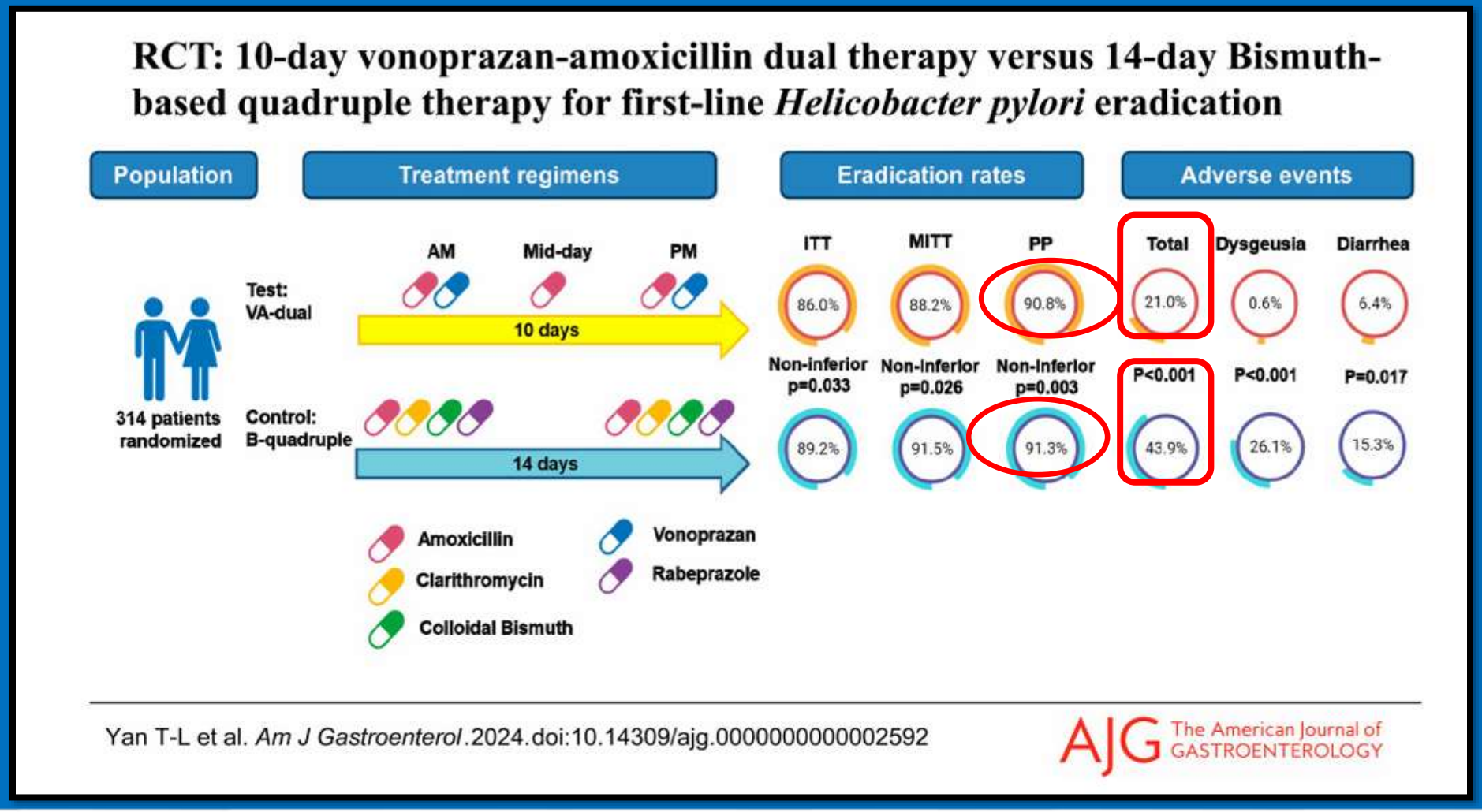
	Time Above pH 4.0 (%)		
	Baseline	Day 1	Day 7
Vonoprazan 20 mg	11%	71%	86%
Esomeprazole 20 mg	11%	24%	61%

RELATIVE POTENCY OF VONOPRAZAN



Tansel A, Graham DY. Gastroenterology. 2023;164(Suppl 1):

Summary



The 10-day VA-dual therapy provided satisfactory eradication rates of >90% (PP analysis) and lower rates of adverse events compared with standard 14-day B-quadruple therapy as first-line *H. pylori* therapy.

Summary

Gastroenterology 2024;167:1228–1238

CLINICAL PRACTICE UPDATES

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

Amit Patel,[1,2] Loren Laine,[3,4] Paul Moayyedi,[5] and Justin Wu[6]

Best Practice Advice 7: Clinicians should use P-CABs in place of PPIs in eradication regimens for most patients with HP infection.

Summary

- P-CAB–based treatment regimens are “non-inferior or superior to conventional PPI-based triple therapies”
- Superior efficacy in patients with antimicrobial resistant infections
- Novel acid blockers … game changer in H. pylori eradication
- Introducing as empirical first-line therapy in treatment naïve patients
- More used in place of PPI due to higher acid suppression
- Waiting long-term safety data, need to weigh benefit and risk


Thank
you