

Helicobacter pylori Resistance Rates in the US and Europe: Data From the pHalcon-HP Study

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OBJECTIVES

To report resistance rates to common *H. pylori* antibiotics across the US and Europe, collected as part of a large clinical trial (pHalcon-HP; NCT04167670).

RESULTS

- ▶ Samples from 907 patients underwent AST.
- ▶ Overall resistance rates to each antibiotic are shown in Table 1.
- ▶ Rates of multi-resistance are displayed in Figure 1.
 - Most patients had strains resistant to at least one antibiotic.
 - One-quarter of patients had no resistant strains.
 - One patient had a strain resistant to all three antibiotics.
- ▶ Baseline characteristics data were generally equally distributed between patients with strains resistant and susceptible to clarithromycin, amoxicillin and metronidazole (Table 2).
- Resistance rates appeared consistently higher among women than men.

Table 1. Overall Resistance Rates in pHalcon-HP (N=907)

	Clarithromycin*	Amoxicillin	Metronidazole
Resistant, n	201	11	628
Susceptible, n	706	896	279
Resistance rate, %	22.2	1.2	69.2

*Clarithromycin susceptibility status was classified as susceptible, intermediate or resistant. For the purpose of this analysis, "clarithromycin-susceptible" refers to patients with strains classified as susceptible or intermediate.

Figure 1. Prevalence of Multi-Resistance in pHalcon-HP

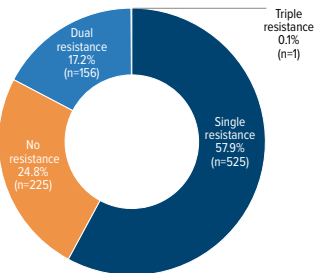


Table 2. Baseline Characteristics and Demographics of Patients with Resistant and Susceptible *H. pylori* Strains

	Clarithromycin-resistant (n=201)	Clarithromycin-susceptible* (n=706)	Amoxicillin-resistant (n=11)	Amoxicillin-susceptible (n=896)	Metronidazole-resistant (n=628)	Metronidazole-susceptible (n=279)
Age, years, mean (SD)	51.5 (13.6)	50.9 (13.6)	54.8 (11.7)	51.0 (13.6)	50.8 (13.8)	51.9 (13.2)
Sex, % (n) female	69.7 (140)	60.5 (427)	81.8 (9)	62.3 (558)	64.0 (402)	59.1 (165)
Race % (n)						
Asian	1.0 (2)	1.7 (12)	9.1 (1)	1.5 (13)	0.8 (5)	3.2 (9)
Black or African American	5.0 (10)	8.5 (60)	0	7.8 (70)	8.0 (50)	7.2 (20)
White	93.0 (187)	87.8 (620)	81.8 (9)	89.1 (798)	90.0 (565)	86.7 (242)
Ethnicity % (n)						
Hispanic or Latino	31.3 (63)	25.6 (181)	54.5 (6)	26.6 (238)	26.1 (164)	28.7 (80)
Not Hispanic or Latino, or unknown	68.7 (138)	74.4 (525)	45.5 (5)	73.4 (658)	73.9 (464)	71.3 (199)
BMI, mean (SD)	29.6 (5.7)	29.5 (6.0)	26.4 (4.7)	29.5 (5.9)	29.3 (5.8)	29.9 (8.3)

*Clarithromycin susceptibility status was classified as susceptible, intermediate or resistant. For the purpose of this analysis, "clarithromycin-susceptible" refers to patients with strains classified as susceptible or intermediate. BMI, body mass index; SD, standard deviation.

- ▶ Resistance rates between the US and Europe were broadly comparable (Figure 2).
- ▶ Clarithromycin resistance was >15% in all US subregions and European countries, except the UK (Figure 3).
- Two US subregions and two European countries had resistance rates to clarithromycin >20%.
- ▶ A total of 4/11 patients with amoxicillin-resistant strains were from one US subregion (US-West).
- ▶ Resistance rates to metronidazole ranged from 54.5% (US-West) to 73.3% (US-Southwest) in the US and from 50.0% (UK) to 79.4% (Bulgaria) in Europe (Figure 4).

Figure 2. Resistance Data by Geographical Location

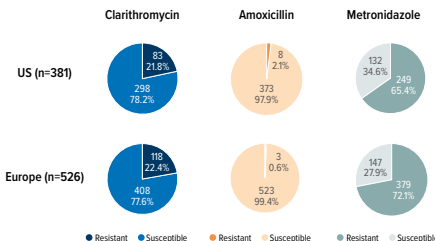


Figure 3. Clarithromycin Resistance by Location

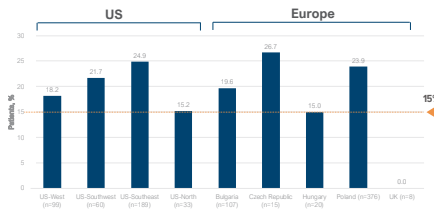
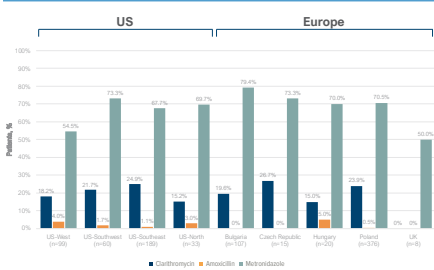


Figure 4. Resistance Rates in the US and Europe



CONCLUSIONS

- ▶ These data, providing a snapshot of resistance rates across the US and Europe, confirm that resistance to metronidazole and clarithromycin is very high in these regions.
- ▶ Clarithromycin resistance rates were >15% in nearly all subregions studied, indicating that empiric use of PPI therapy in these regions should be abandoned.^{2,3}
- ▶ These resistance levels highlight the need to improve antimicrobial stewardship and reduce the risk of further resistance acquisition.
- ▶ A limitation is that these data were collected as part of a large clinical trial, not primarily designed to assess resistance rates. Some subgroups were small, limiting interpretation.
- ▶ Overall, these data provide robust evidence that common treatment practices in the US and Europe should be re-assessed, and responsible antibiotic stewardship emphasized.

BACKGROUND

- ▶ *Helicobacter pylori* infection is common globally, including in the US, where roughly a third of adults have the infection.^{1,2}
- ▶ *H. pylori* is the leading cause of chronic gastritis, peptic ulcers and gastric cancer.^{2,3}
- ▶ Eradication rates with common treatment regimens have been falling due to increasing antimicrobial resistance.^{4,5}
- ▶ The prevalence of resistant strains varies geographically and is an important characteristic to consider when selecting treatment.^{2,3} Both the American College of Gastroenterology (ACG) and Maastricht guidelines recommend that proton pump inhibitor (PPI)-based triple therapy (PPI + clarithromycin + amoxicillin) not be used in areas where clarithromycin resistance is >15% or unknown.^{2,3}
- ▶ In some countries, including the US, local resistance rate information is very limited.⁶

METHODS

- ▶ **pHalcon-HP:** Phase 3 clinical trial investigating the efficacy and safety of vonoprazan triple (vonoprazan, amoxicillin, and clarithromycin) and dual (vonoprazan and amoxicillin) therapies versus lansoprazole triple therapy for the eradication of *H. pylori* infection in patients from the US and Europe.
- ▶ **Patients and biopsy sampling:** Patients ≥18 years old had gastric biopsies systematically collected endoscopically. One biopsy was taken from the greater curve of the antrum and one from the lesser curve of the gastric body.
- ▶ **Isolation and identification of *H. pylori* strains:** Cultured samples with small, gray, and translucent colonies were Gram-stained. Colonies of Gram-negative curved rods with positive oxidase, catalase, and urease tests were submitted for antimicrobial susceptibility testing (AST).
- ▶ **AST:** Minimum inhibitory concentrations of amoxicillin, clarithromycin, and metronidazole were determined for each isolate using agar dilution. Resistance breakpoints used were clarithromycin ≥1 µg/mL, amoxicillin >0.125 µg/mL, and metronidazole >8 µg/mL.
- ▶ **Statistical analyses:** Descriptive statistics were used to report resistance rates by region (US/Europe), US subregion (determined by center location), and European country. Baseline demographics and characteristics of patients with resistant and non-resistant strains were summarized.

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Conflicts of Interest

F. Mégraud received grants from Allergan, Boehringer and Mabring. He is also a consultant for Phathom Pharmaceuticals. D.Y. Graham is a consultant for RedBull BioPharma and Phathom Pharmaceuticals regarding novel *H. pylori* therapies and has received research support for culture of *Helicobacter pylori*. He is also a consultant for DiSolon regarding *H. pylori* diagnostics and with Otsuka Japan regarding novel breath tests. He has ongoing collaborative research projects with American Molecular regarding molecular diagnostics for *H. pylori*. C.W. Howden is a consultant to Phathom Pharmaceuticals, RedBull BioPharma, Homewood and Alliant, and a speaker for RedBull BioPharma and Anyam. He owns stock in AmBio Therapeutics. E. Trevino and A. Weissfeld are employees of Microbiology Specialists, Incorporated, funded by Phathom Pharmaceuticals to undertake this work. B. Hunt, N. Smith and E. Leifke are employees of Phathom Pharmaceuticals. E. Leifke also discloses stockholder interest in Phathom Pharmaceuticals. W.D. Chey discloses being a Board member of the American College of Gastroenterology. G. Di Bonavent, the International Foundation of Functional GI Disorders, and the Rome Foundation, compensation as a consultant from Abbvie, Allergan, Alliant, Anyam, Bayer, Boehringer, Celonis, Intertec Medicine, Inverwood Pharmaceuticals, QOL Medical, Nestle, Phathom Pharmaceuticals, RedBull BioPharma, Sankyo, Watson, Takeda, Uovisat, and Varian; grant/research support from Boehringer, Commonwealth Diagnostic International, QOL Medical, Sankyo, and Varian; stock/stock options in G. Di Bonavent, and Moddy Health; and patients relating to My GI Health, My Nutrition Health, digital manometry and a rectal expansion device.

Meeting details

Presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting 2021, Las Vegas, October 22–27