

Clarithromycin Resistance and *H pylori* Eradication Rates in US Racial Groups With Rabeprazole-Based Triple Therapy

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Background and Objective

Resistance to clarithromycin may compromise the efficacy of triple-therapy regimens for the eradication of *Helicobacter pylori*. If clarithromycin resistance could be predicted based on patient demographics, it would help clinicians tailor regimens for *H pylori* eradication. For this reason, we analyzed clarithromycin resistance across different racial groups in a large-scale efficacy trial of triple therapy with rabeprazole, amoxicillin, and clarithromycin.

Methods

Study Design and Patients

- Multicenter, double-blind, controlled, randomized, parallel-group trial.
- 803 randomized patients, aged 18 years or older, with 1:1 stratification of patients with peptic ulcer disease (PUD) and non-peptic ulcer disease (NPUD).
- Patients enrolled had *H pylori* infection documented by *H pylori* antibody and ¹³C-urea breath test (¹³C-UBT), and either *Campylobacter*-like organism (CLO) test or *H pylori* culture.
- Patients received 1 of 4 triple-therapy regimens: rabeprazole 20 mg bid, amoxicillin 1 g bid, and clarithromycin 500 mg bid for 3, 7, or 10 days (RAC-3, -7, -10) or a control regimen of omeprazole 20 mg bid plus the same antibiotics for 10 days (OAC-10).

Efficacy Criteria

- The primary efficacy variable was eradication of *H pylori* as measured by negative ¹³C-UBT for *H pylori* ≥42 days from the end of treatment.
- Eradication rates were assessed overall and by race.

Assessment of Resistance

- Pretreatment screening for antimicrobial sensitivity was conducted on *H pylori* isolated from gastric biopsies.
- Screening used the agar dilution method of the National Committee for Clinical Laboratory Standards standardized susceptibility testing procedures.
- Clarithromycin susceptibility using minimum inhibitory concentration (MIC) values was defined as:
 - Sensitive: MIC ≤0.25 µg/mL
 - Intermediate: MIC 0.5 µg/mL
 - Resistant: MIC ≥1.0 µg/mL
- Subgroup analysis examined pretreatment clarithromycin susceptibility as a function of race: African American, Caucasian, Hispanic, and Other.

Statistical Methods

- Therapeutic equivalence between treatments was assessed via 2-sided 95% confidence interval (CI) for the difference in eradication rates between OAC and each of the 3 RAC regimens. Equivalence was defined as 2-sided 95% CI in the range of -15%, 15%.
- Susceptibility by race was determined by logistic regression analysis with analysis of variance for maximum likelihood of group variation. Logistic regression analysis was also used to determine eradication rates by race.

Results

- Efficacy evaluable population: N = 783 intent-to-treat (ITT); N = 683 per protocol (PP). Hispanic patients represented the largest racial group (n = 252) (Table).
- Results of pretreatment antimicrobial sensitivity testing, available in 560 of 783 ITT patients, showed that 51 isolates (9.1%) were resistant and 2 (0.4%) were intermediate to clarithromycin. In this trial, amoxicillin resistance occurred in only 2 isolates (0.4%), both of which were also clarithromycin resistant.
- Pretreatment clarithromycin susceptibility for different racial groups is shown in Figure 1. Logistic regression analysis found no association between patients' race and clarithromycin sensitivity (P = 0.48).

- Race had no effect on *H pylori* eradication rates with rabeprazole-based triple therapy (logistic regression analysis). Eradication rates by racial group are depicted in Figure 2 (ITT) and Figure 3 (PP).
- Overall eradication rates with RAC-7 and RAC-10 were high, and equivalent to rates with OAC-10; efficacy with RAC-3 was low.
- All regimens were well tolerated. Taste disturbance was reported by significantly fewer RAC-7 patients than OAC-10 patients (P ≤0.05).

Table. Patient Demographics

	RAC-3 (n = 194)	RAC-7 (n = 200)	RAC-10 (n = 202)	OAC-10 (n = 207)
Age, mean years±SEM	45.1±1.05	46.9±0.95	48.2±0.92	45.6±0.94
Gender, n female (%)	111 (57)	106 (53)	106 (52)	118 (57)
Race, n (%)				
Hispanic	86 (44)	93 (47)	88 (44)	88 (43)
Caucasian	69 (36)	74 (37)	83 (41)	84 (41)
African American	33 (17)	26 (13)	20 (10)	27 (13)
Asian	4 (2)	6 (3)	5 (2)	6 (3)
Other	2 (1)	1 (<1)	6 (3)	2 (<1)
Stratified to PUD, n (%)	93 (48)	103 (52)	100 (50)	104 (50)

SEM = standard error of the mean.

Figure 1. Pretreatment Clarithromycin Susceptibility by Race (% of ITT Tested Patients)

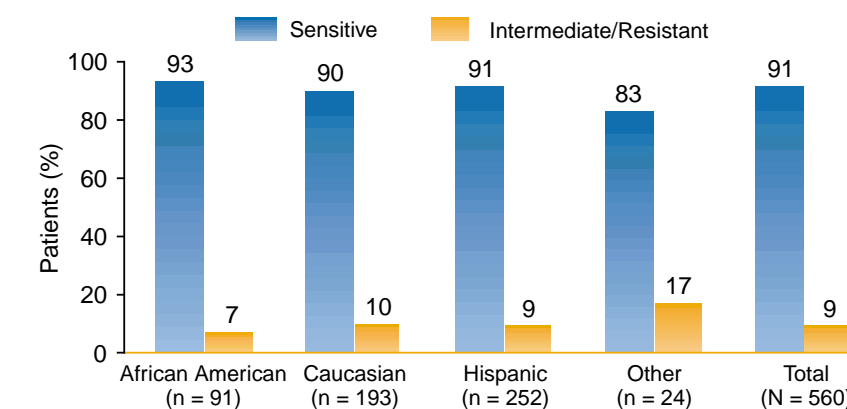


Figure 2. *H pylori* Eradication Rates by Race, ITT Patients (N = 783)

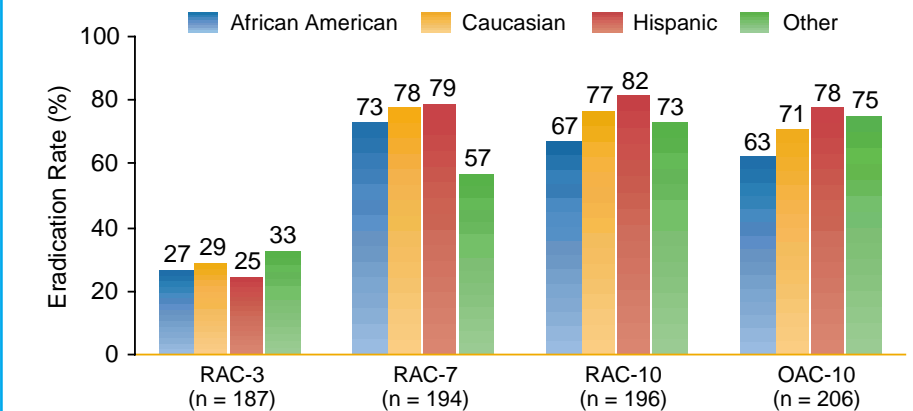
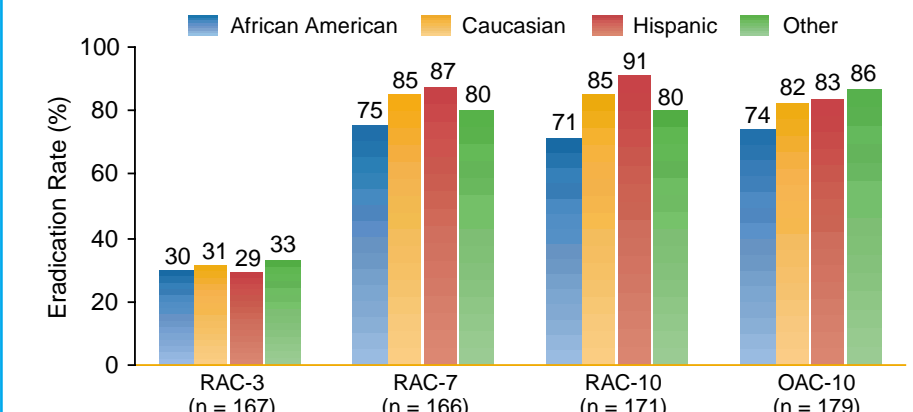


Figure 3. *H pylori* Eradication Rates by Race, PP Patients (N = 683)



Conclusions

- Race was not associated with differences in either pretreatment clarithromycin resistance or *H pylori* eradication rates with RAC or OAC regimens.
- Primary treatment regimens should not vary based on race in the United States.
- RAC-7 produced efficacy equivalent to OAC-10 with less taste disturbance, indicating a possible therapeutic advantage for the shorter course RAC-7.