

Low-dose Rifabutin (50 mg) Triple Therapy for *H. pylori* Is Efficacious and Well Tolerated in Patients with Obesity or Diabetes

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BACKGROUND

- The overall US prevalence of *Helicobacter pylori (H. pylori)* infection is ~35% but higher among non-Hispanic Black and Mexican Americans.^{1,2}
- □ The estimated prevalence of obesity in non-Hispanic Black adults is 49.9% and 45.6% in Hispanic adults.³
- The estimated prevalence of diabetes in non-Hispanic Blacks is 12.1% and 11.8% in Hispanics.⁴
- *H. pylori* eradication has become more challenging due to rising antibiotic resistance.⁵⁻⁷
- Diabetes and obesity may further complicate the successful treatment of the infection.⁸⁻¹²
- □ A meta-analysis confirmed a higher risk of *H. pylori* eradication failure in patients with diabetes vs. those without diabetes.
- Total diabetes prevalence in the US is estimated to be 11.3%⁴, which is mostly type 2 diabetes.
- Obesity decreases the efficacy of clarithromycin triple therapy by nearly 50%.¹²
- A potential contributing factor to eradication success is intragastric antibiotic concentration time at or above the MIC₀₀ for *H. pylori*.¹⁴

OBJECTIVES

• We aimed to assess if the efficacy of low-dose rifabutin (50 mg Q8H) triple therapy, RHB-105 (Talicia[®]) (50 mg rifabutin, 1000 mg amoxicillin, 40 mg omeprazole, Q8H for 14 days) for *H. pylori* infection was affected by patient obesity or diabetic

METHODS

- We conducted a *post hoc* analysis of pooled, modified-intent to treat data from 293 subjects in the Phase 3 RHB-105 clinical trials (NCT01980095/NCT03198507) analyzing the efficacy and safety of RHB-105 for *H. pylori* infection.
- We compared *H. pylori* eradication rates, safety, demographics, and body mass index (BMI) in patients with and without diabetes
- We used physiologically based pharmacokinetic (PBPK) modeling to assess intragastric antibiotic concentration time above the MIC₉₀ for *H. pylori* (0.008 μ g/ml) in normal, overweight, and obese patients.

RES	ULT	'S										STUDY 1		STUDY 2		POOLED			
														With Diabetes	Without Diabetes	With Diabetes	Without Diabetes	With Diabetes	Wit
Ji the 293 subjects, 84% were white; 68% were Hispanic; 59% were women. Average BIVII was 30.5 kg/m². Patients with Jiabetes (n=48) were older (54 vs. 45 years), were more often black or African American (21% vs. 12%) and had higher BMI												Adverse Reaction	N=12	N=65	N=38	N=190	N=50		
33 vs. 30 kg/m ²) compared to patients without diabetes (n=245).													Diarrhea	0 (0.0%)	11 (16.9%)	3 (7.9%)	20 (10.5%)	3 (6.0%)	
Table 1: S	able 1: Subject Demographics Between Patients With and Without Diabetes													1 (8.3%)	9 (13.8%)	4 (10.5%)	13 (6.8%)	5 (10.0%)	
		SEX		AGE	BMI	RACE		ACE	ETHNICITY				Nausea	0 (0.0%)	3 (4.6%)	4 (10.5%)	7 (3.7%)	4 (8.0%)	
Diabetes		Μ	F			White	Black/ AA	Native American	Other	Hispanic	Non-Hispanic	N	Abdominal Pain	1 (8.3%)	1 (1.5%)	1 (2.6%)	3 (1.6%)	2 (4.0%)	
No	n	101	144	44.6	30.1	210	29	1	5	167	78	045	Chromaturia	1 (8.3%)	9 (13.8%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	
	%	41%	59%			86%	12%	0%	2%	68%	32%	245	Rash	0 (0.0%)	2 (3.1%)	1 (2.6%)	2 (1.1%)	1 (2.0%)	
Yes	n	19	29	53.9	32.6	35	10	1	2	32	16		Dyspepsia	0 (0.0%)	1 (1.5%)	1 (2.6%)	3 (1.6%)	1 (2.0%)	
	%	40%	60%			73%	21%	2%	4%	67%	33%	48	Vomiting	0 (0.0%)	1 (1.5%)	0 (0.0%)	6 (3.2%)	0 (0.0%)	
AA: African American											Oropharyngeal Pain	0 (0.0%)	3 (4.6%)	0 (0.0%)	2 (1.1%)	0 (0.0%)			
													Vulvovaginal Candidiasis	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (0.5%)	1 (2.0%)	

diabetes, respectively (Figure 1).



For more detailed information, please contact the Medical Affairs Team at RedHill Biopharma at: medinfo@redhillus.com

4 (1.8%)

9 (4.0%)

4 (1.8%)

4 (1.8%)

7 (3.1%)

5 (2.2%)

1 (0.4%)

0.10

Normal BMI: 18.5<BMI<24.9

Time (hrs)

Overweight: 25<BMI<29.9

Obese: BMI>30

Figure 3 represents day 6 (steady state) of a 14 day therapy.

———— MIC₉₀ (0.008 mcg/mL)





CONCLUSIONS

- Low-dose rifabutin (50mg Q8H) triple therapy for 14 days produced high eradication rates and displayed favorable safety and tolerability across all subjects.
- Despite higher mean age and BMI, and a different racial and ethnic distribution in patients with vs. without diabetes, eradication rates with RHB-105 remained high supporting its use in populations with unmet needs.
- PBPK modeling supports minimal differences in intragastric rifabutin concentration time above MIC_{oo} for *H. pylori* between patients with normal BMI or who are overweight or obese, supporting the minimal differences seen in eradication outcomes with RHB-105 between patients irrespective of BMI status.
- This study supports the efficacy and safety of low-dose rifabutin triple therapy as empiric first-line treatment for *H. pylori* infection in patients regardless of obesity or diabetic status.

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