DDW2022
Digestive Disease Week®
MAY 21-24 | SAN DIEGO, CA

Low-Dose Rifabutin Triple Therapy (RHB-105) Maintains High *Helicobacter pylori (H. pylori)* Eradication Rates and Shows Favorable Safety and Efficacy in Subjects with Diabetes Mellitus

Poster Number
Tu1078

C. Howden[1], B. Johns[2], J. Almenoff[3] and K. Sheldon[3]
[1]University of Tennessee College of Medicine, Memphis, TN
[2]The Jones Center for Diabetes and Endocrine Wellness, Macon, GA
[3]RedHill Biopharma, Medical Affairs, Raleigh, NC

INTRODUCTION

- Estimated US prevalence of *H. pylori* ~35%.[1]
- Success rates with clarithromycin-containing regimens have fallen largely due to increasing clarithromycin resistance.[2,3,4]
- ACG guidelines recommend that clarithromycin triple therapies should be avoided in patients who have previously received a macrolide, and where local clarithromycin resistance rates are ≥15% or unknown.[5]
- Clarithromycin use persists despite a general lack of information about local *H. pylori* resistance and the susceptibility of individual strains to it.[3]
- An additional, potential contributing factor to clarithromycin failure is diabetes mellitus (DM); clarithromycin based therapies are more likely to fail in patients with DM than in those without.[6,7]
- Over 37.3 million Americans are estimated to have DM (11.3% of the US population).[8]
- Because of the high failure rate of clarithromycin therapies in those with DM, it is important to evaluate alternative treatment options for *H. pylori*.
- RHB-105 is formulated as an all-in-one combination of low-dose rifabutin triple therapy (rifabutin 50 mg / amoxicillin 1000 mg / omeprazole 40 mg) as 4 capsules to be given Q8H for 14 days for the treatment of *H. pylori* infection in adults.
- RHB-105 was proven safe and efficacious in two Phase 3 trials (ERADICATE Hp [NCT01980095]; ERADICATE Hp2 [NCT03198507]). Eradication rates in Phase 3 trials: [9,10,11]
  - ERADICATE Hp: 89.4% for RHB-105 vs. 70% for literature-derived comparator rate ($p<0.001$) in the modified intent-to-treat population (mITT).[a,b,c]
  - ERADICATE Hp2: 84.1% for RHB-105 vs. 57.7% for amoxicillin 1000 mg and omeprazole 40 mg Q8H ($p<0.001$) in mITT and 90.3% for confirmed adherent population vs 64.7% for the same comparator ($p<0.001$).

[a]Clarithromycin, amoxicillin, and proton pump inhibitor (omeprazole or lansoprazole).
[b]Metronidazole, bismuth subcitrate potassium, and tetracycline.
[c]Bismuth subcitrate potassium, metronidazole, tetracycline, and omeprazole.

OBJECTIVE

- To evaluate any potential impact of diabetes on the efficacy and safety of RHB-105.

METHODS

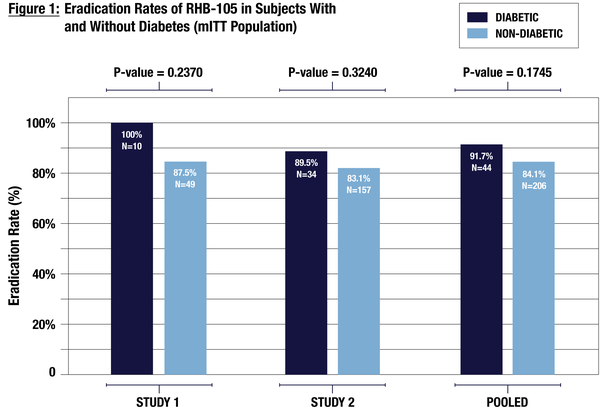
- Data were pooled from the two Phase 3 clinical studies with RHB-105.[9,10]
  - Studies included treatment-naïve subjects with confirmed *H. pylori* infection; eradication was verified using a ^{13}C-urea breath test at least 4 weeks after completion of therapy.
- A *post-hoc* analysis based on presence or absence of DM was performed on the pooled mITT population. *H. pylori* isolates from treatment-naïve subjects in Study 2 were tested for antibiotic resistance.

RESULTS

EFFICACY

- The mITT population included 293 analyzable subjects in this *post-hoc* analysis.
- Pooled eradication rates of those subjects receiving RHB-105 were 91.7% (95% CI 80.4-96.7) and 84.1% (95% CI 79.0-88.1) in subjects with and without DM, respectively ($P = 0.1745$; Figure 1).
- There were no significant differences in eradication rates between subjects with and without DM in the individual studies or in the pooled analysis.

Figure 1: Eradication Rates of RHB-105 in Subjects With and Without Diabetes (mITT Population)



RESISTANCE

- There were similar rates of resistance between subjects with and without DM for rifabutin, clarithromycin, metronidazole, and amoxicillin (0% vs. 0%, 21.0% vs. 17.0%, 45.0% vs. 43.0%, and 4.0% vs. 7.0%) (Table 1).
- Presence of DM did not have a significant impact on antibiotic resistance profiles, and resistance rates were similar to the overall study (rifabutin 0%, clarithromycin 17.4%; metronidazole 43.6%; and amoxicillin 6.4%).

Table 1: Resistance Rates of Subjects With and Without Diabetes (mITT Population)

ANTIBIOTIC/ N (%)	SUCCEPTABILITY	WITH DIABETES	WITHOUT DIABETES
Rifabutin	Susceptible	53 (100.0)	292 (100.0)
	Resistant	0	0
	Missing	16	94
Clarithromycin	Susceptible	42 (79.0)	242 (83.0)
	Resistant	11 (21.0)	49 (17.0)
	Missing	16	94
Metronidazole	Susceptible	29 (55.0)	164 (57.0)
	Resistant	24 (45.0)	126 (43.0)
	Missing	16	95
Amoxicillin	Susceptible	51 (96.0)	271 (93.0)
	Resistant	2 (4.0)	20 (7.0)
	Missing	16	94

SAFETY

- Generally, the safety and tolerability of RHB-105 was similar between groups (Table 2).
- Presence of DM did not have a considerable impact on the safety and tolerability of RHB-105 and generally matched the profile seen in the total population.

Table 2: Safety and Tolerability of Subjects With and Without Diabetes (mITT Population)

ADVERSE EVENTS N (%)	STUDY 1		STUDY 2		POOLED	
	DIABETIC (N=12)	NON-DIABETIC (N=65)	DIABETIC (N=38)	NON-DIABETIC (N=190)	DIABETIC (N=50)	NON-DIABETIC (N=225)
Diarrhea	0	11 (16.9)	3 (7.9)	20 (10.5)	3 (6.0)	31 (13.8)
Headache	1 (8.3)	9 (13.8)	4 (10.5)	13 (6.8)	5 (10.0)	22 (9.8)
Nausea	0	3 (4.6)	4 (10.5)	7 (3.7)	4 (8.0)	12 (5.3)
Abdominal pain	1 (8.3)	1 (1.5)	1 (2.6)	3 (1.6)	2 (4.0)	4 (1.8)
Chromaturia	1 (8.3)	9 (13.8)	0	0	1 (2.0)	9 (4.0)
Rash	0	2 (3.1)	1 (2.6)	2 (1.1)	1 (2.0)	4 (1.8)
Dyspepsia	0	1 (1.5)	1 (2.6)	3 (1.6)	1 (2.0)	4 (1.8)
Vomiting	0	1 (1.5)	0	6 (3.2)	0	7 (3.1)
Oropharyngeal pain	0	3 (4.6)	0	2 (1.1)	0	5 (2.2)
Vulvovaginal candidiasis	0	0	1 (2.6)	1 (0.5)	1 (2.0)	1 (0.4)
Urinary tract infection	1 (8.3)	0	2 (5.3)	0	3 (6.0)	0

REFERENCES

1. Hooi JKY, et. Al. Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis. *Gastroenterology*. 2017; 153(2):420-429.
2. Argueta EA, et al. Impact of Antimicrobial Resistance Rates on Eradication of *Helicobacter pylori* in a US Population. Gastroenterology. 2021; 160(6), 2181-2183.
3. Howden CW, et al. Pitfalls of Physician-Directed Treatment of *Helicobacter pylori*: Results from Two Phase 3 Clinical Trials and Real-World Prescribing Data [published online ahead of print, 2021 Dec 4]. *Dig Dis Sci*. 2021;10.1007/s10620-021-07323-5.
4. Park JY, et al. *Helicobacter pylori* Clarithromycin Resistance and Treatment Failure Are Common in the USA. *Dig Dis Sci*. 2016;61(8):2373-2380.
5. Chey WD, et al. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection [published correction appears in Am J Gastroenterol. 2018 Jul;113(7):1102]. *Am J Gastroenterol*. 2017;112(2):212-239.
6. Horikawa C, et al. High risk of failing eradication of *Helicobacter pylori* in patients with diabetes: a meta-analysis. *Diabetes Res Clin Pract*. 2014;106(1):81-87.
7. Yao CC, et al. First-line *Helicobacter pylori* eradication rates are significantly lower in patients with than those without type 2 diabetes mellitus. *Infect Drug Resist*. 2019;12:1425-1431.
8. Centers for Disease Control and Prevention. National Diabetes Statistics Report website. https://www.cdc.gov/diabetes/data/statistics-report/index.html. Accessed April 13, 2022.
9. Graham DY, et al. Rifabutin-Based Triple Therapy (RHB-105) for *Helicobacter pylori* Eradication: A Double-Blind, Randomized, Controlled Trial. *Ann Intern Med*. 2020;172(12):795-802.
10. Kalfus IN, et al. Rifabutin-Containing Triple Therapy (RHB-105) for Eradication of *Helicobacter pylori*: Randomized ERADICATE Hp Trial. *Antibiotics (Basel)*. 2020;9(10):685.
11. Talicia. Prescribing Information. Raleigh, NC: RedHill Biopharma; Version 3/2022.

ACKNOWLEDGMENTS
Medical writing support was provided by Philip Yeung from Medical Affairs 360, LLC. (Carlsbad, CA, USA).

CONCLUSION

- In this post hoc analysis, the efficacy of RHB-105 was maintained in subjects with DM and was not statistically significantly different from that in subjects without DM.
- Resistance rates for all antibiotics tested were similar in subjects with and without DM. No isolates showed resistance to rifabutin.
- Since low-dose rifabutin triple therapy, RHB-105, maintains high eradication rates and is well tolerated regardless of DM status, it represents a rational first-line choice for the treatment of *H. pylori* infection.

QR CODE

Please use the provided QR Code to the right, for the online version of this poster for more depth and insight into the study.

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