D0100

Efficacy and Safety of RBX2660 in Patients After First Recurrence of *Clostridioides difficile* Infection – Results From a Randomized, Placebo-Controlled, Phase 3 Study

Sahil Khanna,[1] Glenn Tillotson,[2] Masakazu Ando,[3] Lindy Bancke,[4] Adam Harvey,[4] Kevin W. Garey,[5] Kerry LaPlante[6]

[1]Mayo Clinic, Rochester, MN, USA; [2]GST Micro, North, VA, USA; [3]Ferring Pharmaceuticals, Parsippany, NJ, USA; [4]Rebiotix Inc., a Ferring Company, Roseville, MN, USA; [5]University of Houston College of Pharmacy, Houston, TX, USA; [6]University of Rhode Island College of Pharmacy, Kingston, RI, USA

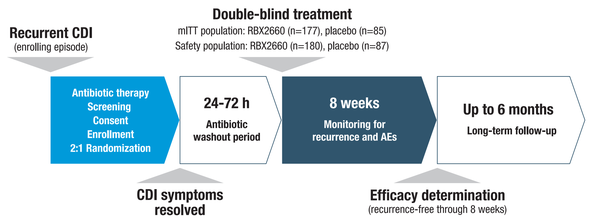
BACKGROUND

- Antibiotics used to treat *Clostridioides difficile* infection (CDI) can damage gut microbiota and increase the risk of CDI[1]
- Gut microbiome restoration by fecal microbiota transplantation is recommended by multiple guidelines after ≥2 episodes of rCDI
- There are no guideline recommendations for microbiome restoration earlier in the course of CDI[2,3]
- RBX2660 is a standardized, microbiota-based live biotherapeutic product being investigated as a treatment option for rCDI[4-6]
- RBX2660 is administered as a single dose via rectal administration, without the need for sedation, colonoscopy, or bowel preparation
- A prespecified analysis of a prospective, multicenter, randomized, double-blind, placebo-controlled, phase 3 trial, PUNCH CD3 (NCT03244644), showed consistent efficacy of RBX2660 in patients with ≤3 (treatment success: placebo, 67%; RBX2660, 72%) and >3 (placebo, 54%; RBX2660, 70%) episodes of CDI before enrollment
- In this post hoc analysis, the efficacy and safety of RBX2660 in patients with 1 rCDI episode (ie, 2 episodes of CDI) before enrollment were assessed

METHODS

- Patients enrolled in PUNCH CD3 were ≥18 years old with ≥1 rCDI episode as determined by the treating physician and assessed with current standard-of-care (SOC) diagnostic methods (**Figure 1**)
- After completing SOC antibiotic therapy for the enrolling CDI episode, patients received a single blinded dose of RBX2660 or placebo
- Treatment success was defined as remaining free of CDI recurrence for 8 weeks after treatment
  - After 8 weeks, patients were monitored for new CDI occurrences through 6 months
- Treatment-emergent adverse events (TEAEs) were summarized for the double-blind treatment period within 8 weeks

Figure 1. PUNCH CD3 Study Design



AE, adverse event; CDI, *Clostridioides difficile* infection; mITT, modified intent-to-treat.

KEY TAKEAWAYS

1. **This study is the first to report on the effects of a live biotherapeutic product in patients who have experienced 1 prior CDI recurrence**
2. **RBX2660-treated patients had numerically higher treatment success at 8 weeks compared with placebo**
3. **In patients who experienced RBX2660 treatment success at 8 weeks, response was sustained through 6 months in 91% of this population**
4. **These results support the efficacy and safety of RBX2660 in reducing rCDI in patients as early as the first CDI recurrence**

RESULTS

- **In the modified intent-to-treat population, 86 of 262 patients (32.8%) were enrolled after 1 rCDI**
- **Patients were mostly White (93.0%) and female (66.3%), with a mean age of 58 years**

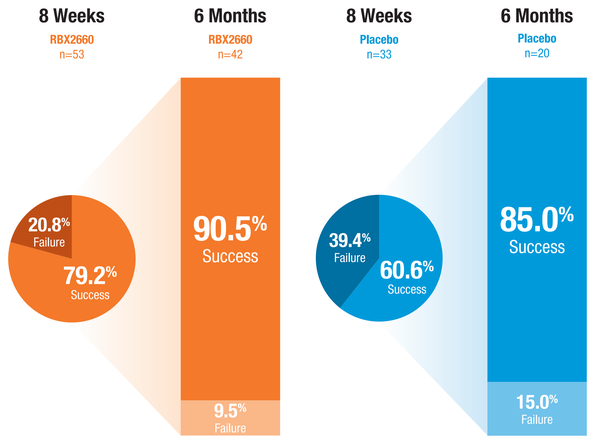
Table 1. Demographics and Baseline Characteristics of Patients With a First Recurrent CDI Episode Before Treatment (mITT Population)

	Placebo n=33	RBX2660 n=53	Total N=86
Age, mean (SD), years	57.8 (15.91)	58.6 (20.10)	58.3 (18.51)
Female, n (%)	22 (66.7)	35 (66.0)	57 (66.3)
White race, n (%)	31 (93.9)	49 (92.5)	80 (93.0)

CDI, *Clostridioides difficile* infection; mITT, modified intent-to-treat.

- **RBX2660-treated patients had numerically higher treatment success at 8 weeks compared with placebo-treated patients**
- **At week 8, 79.2% of RBX2660-treated patients and 60.6% of placebo-treated patients achieved treatment success**
- **Of the patients who experienced RBX2660 treatment success at 8 weeks, 90.5% treated with RBX2660 and 85% treated with placebo remained recurrence-free at 6 months**

Figure 2. Subgroup Analysis of Patients Enrolled Following a First rCDI Episode: Treatment Success at 8 Weeks and in Treatment Responders at 6 Months



	8 Weeks		6 Months	
	RBX2660 n=53	Placebo n=33	RBX2660 n=42	Placebo n=20
Success, n (%)	42 (79.2)	20 (60.6)	38 (90.5)	17 (85.0)
Failure, n (%)	11 (20.8)	13 (39.4)	4 (9.5)	3 (15.0)

rCDI, recurrent *Clostridioides difficile* infection.

Table 2. Overall Summary of Adverse Events for Patients With a First Recurrent CDI Episode Before Treatment (Safety Population)[a]

Event, n (%)	Placebo n=33	RBX2660 n=53
All TEAEs	11 (33.3)	29 (54.7)
Mild TEAEs	1 (3.0)	12 (22.6)
Moderate TEAEs	6 (18.2)	11 (20.8)
Severe TEAEs	4 (12.1)	6 (11.3)
Potentially life-threatening TEAEs	0 (0.0)	0 (0.0)
TEAEs leading to discontinuation	0 (0.0)	0 (0.0)
SAEs	2 (6.1)	3 (5.7)

CDI, *Clostridioides difficile* infection; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

[a]Severity is presented by maximum severity per patient.

- **TEAEs were reported by 54.7% of RBX2660-treated patients and 33.3% of placebo-treated patients**
  - **The difference between groups was mostly due to mild events (by maximum severity)**
  - **Overall, TEAEs were typically mild to moderate in severity and comprised mainly gastrointestinal events (predominantly diarrhea and abdominal pain)**
- **Serious adverse events were reported by 5.7% of RBX2660-treated and 6.1% of placebo-treated patients**
- **No potentially life-threatening TEAEs or TEAEs leading to discontinuation or death were reported**

References

1. Chaar A, Feuerstadt P. *Therap Adv Gastroenterol.* 2021;14:17562848211011953.
2. Johnson S, et al. *Clin Infect Dis.* 2021;73(5):e1029-e1044.
3. Kelly CR, et al. *Am J Gastroenterol.* 2021;116(6):1124-1147.
4. Orenstein R, et al. *Clin Infect Dis.* 2016;62:596-602.
5. Langdon A, et al. *Genome Med.* 2021;13:28.
6. Orenstein R, et al. *BMC Infect Dis.* 2022;22(1):245.

Acknowledgments

The authors thank all the participants and their families and caregivers and the investigators and site staff. Medical writing assistance was provided by ApotheCom (Yardley, PA, USA) and was funded by Ferring Pharmaceuticals (Parsippany, NJ, USA).

This study was supported by Ferring Pharmaceuticals.

Contact Information

For comments and questions, contact khanna.sahil@mayo.edu.

Presented at American College of Gastroenterology (ACG) 2022 Annual Scientific Meeting and Postgraduate Course; October 21-26, 2022; Charlotte, North Carolina