D0098

Efficacy and Safety of RBX2660 in Patients With Recurrent *Clostridioides difficile* Infection Grouped by Age and Underlying Comorbidities

Paul Feuerstadt,[1] Glenn Tillotson,[2] Laurie Archbald-Pannone,[3] Stuart Johnson,[4,5] Samson Ng,[6] Masakazu Ando,[6] Adam Harvey[7]

[1]Yale University School of Medicine and PACT Gastroenterology Center, Hamden, CT, USA; [2]GST Micro, North, VA, USA; [3]University of Virginia, Charlottesville, VA, USA; [4]Edward Hines, Jr. VA Hospital, Hines, IL, USA; [5]Loyola University Medical Center, Maywood, IL, USA; [6]Ferring Pharmaceuticals, Parsippany, NJ, USA; [7]Rebiotix Inc., a Ferring Company, Roseville, MN, USA

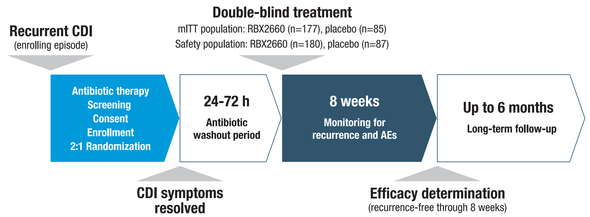
BACKGROUND

- Age and certain underlying comorbidities are among the risk factors for recurrent *Clostridioides difficile* infection (rCDI)[1,2]
- Microbiota-restoring approaches are being widely evaluated for the treatment of rCDI in controlled clinical studies[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
- The Charlson Comorbidity Index (CCI) is a commonly used index that incorporates a subset of 16 conditions and age to predict long-term mortality based on comorbidity burden[7]
- In this post hoc subgroup analysis of PUNCH CD3 (NCT03244644), a prospective, multicenter, randomized, double-blind, placebo-controlled, phase 3 trial, we report the efficacy and safety of RBX2660 in participants with rCDI grouped by age and baseline CCI severity scores

METHODS

- Participants enrolled in PUNCH CD3 were ≥18 years old with ≥1 documented episode of rCDI who completed standard-of-care antibiotic therapy before treatment with RBX2660 or placebo (**Figure 1**)
- Treatment success was defined as remaining free of CDI recurrence 8 weeks after treatment
- In this post hoc subgroup analysis, we assessed the 8-week outcomes of participants grouped by age (<65 years, 65 to 74 years, and ≥75 years) and CCI severity scores at screening (0 to 2 [mild], 3 or 4 [moderate], and ≥5 [severe])
- Treatment-emergent adverse events (TEAEs) were defined as any adverse event occurring on or after blinded treatment
- TEAEs were summarized for the double-blind treatment period within 8 weeks and censored if a participant received open-label RBX2660 after CDI recurrence

Figure 1. PUNCH CD3 Study Design



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

KEY TAKEAWAYS

1 RBX2660 was efficacious across participants with ≥1 rCDI grouped by age and underlying comorbidity burden

2 RBX2660 was well tolerated across subgroups, with most TEAEs being gastrointestinal in nature and mild or moderate in severity

3 These data highlight the consistent efficacy and safety of RBX2660 across a wide range of patients with rCDI, including those with underlying comorbidities

RESULTS

Table 1. Demographics and Baseline Characteristics (mITT population)

	RBX2660 n=177	Placebo n=85	Total N=262
Age, n (%)			
<65 years	90 (50.8)	53 (62.4)	143 (54.6)
65-74 years	46 (26.0)	22 (25.9)	68 (26.0)
≥75 years	41 (23.2)	10 (11.8)	51 (19.5)
Female, n (%)	122 (68.9)	59 (69.4)	181 (69.1)
Charlson Comorbidity Index category, n (%)			
<3	68 (38.4)	39 (45.9)	107 (40.8)
≥3	109 (61.6)	46 (54.1)	155 (59.2)
Number of CDI episodes before blinded treatment, n (%)			
≤3	111 (62.7)	57 (67.1)	168 (64.1)
>3	66 (37.3)	28 (32.9)	94 (35.9)

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

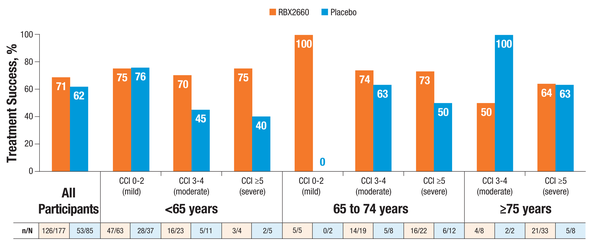
Figure 2. Summary of Treatment Success (mITT population)

CCI, Charlson Comorbidity Index; mITT, modified intent-to-treat.

PUNCH CD3 participants with treatment success (success = orange) or treatment failure (nonsuccess = blue) at week 8 are plotted according to age and baseline CCI score. Each circle represents a unique participant.

- In the total mITT population, 71% of RBX2660-treated participants achieved treatment success compared with 62% of placebo-treated participants
- RBX2660 treatment success rates were consistent across most subgroups
- A greater percentage of RBX2660-treated participants remained free of CDI recurrence through 8 weeks following treatment compared with placebo-treated participants in most subgroups

Figure 3. Summary of Treatment Success Across Subgroups (mITT population)

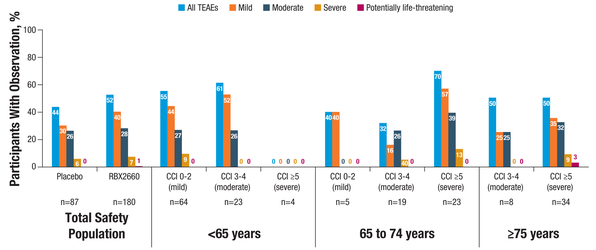


CCI, Charlson Comorbidity Index; CDI, *Clostridioides difficile* infection; mITT, modified intent-to-treat.

RBX2660 treatment success (orange) compared with placebo treatment success (blue) in subgroups based on age and baseline CCI severity scores. Success is defined as remaining free of CDI recurrence through 8 weeks after treatment. The low number of participants in some subgroups may limit data interpretation.

- RBX2660 treatment was successful across a range of participant ages and comorbidity burdens

Figure 4. Summary of Adverse Events Across Subgroups



CCI, Charlson Comorbidity Index; CDI, *Clostridioides difficile* infection; TEAE, treatment-emergent adverse event.

TEAEs were summarized for the double-blind treatment period within 8 weeks and censored if a participant received open-label RBX2660 after CDI recurrence.

- Across subgroups, most TEAEs were mild or moderate in severity

Table 2. Summary of Serious Adverse Events Across Subgroups

	Total Safety Population	RBX2660 Safety Population								
			<65 years			65-74 years			≥75 years	
	Placebo n=87	RBX2660 n=180	CCI 0-2 (mild) n=64	CCI 3-4 (moderate) n=23	CCI ≥5 (severe) n=4	CCI 0-2 (mild) n=5	CCI 3-4 (moderate) n=19	CCI ≥5 (severe) n=23	CCI 3-4 (moderate) n=8	CCI ≥5 (severe) n=34
Serious AEs,[a] n (%)	4 (4.6)	9 (5.0)	3 (4.7)	0	0	0	0	2 (8.7)	0	4 (11.8)
AEs leading to discontinuation, n (%)	0	1 (0.6)[b]	0	0	0	0	0	0	0	1 (2.9)[b]
TEAEs leading to death, n (%)	0	1 (0.6)[b,c]	0	0	0	0	0	0	0	1 (2.9)[b,c]

AE, adverse event; CCI, Charlson Comorbidity Index; CDI, *Clostridioides difficile* infection; TEAE, treatment-emergent adverse event.

TEAEs were summarized for the double-blind treatment period within 8 weeks and censored if a participant received open-label RBX2660 after CDI recurrence.

[a]The serious AEs reported were cardiorespiratory arrest (n=1), abdominal pain (n=1), diarrhea (n=1), ileus (n=1), asthenia (n=1), cellulitis (n=2), *C. difficile* colitis (n=2), CDI (n=2), abdominal abscess (n=1), hand fracture (n=1), postoperative ileus (n=1), dehydration (n=1), failure to thrive (n=1), and alcohol withdrawal syndrome (n=2). *C. difficile* colitis and CDI events were classified as serious AEs because of hospitalization.

[b]The AE leading to discontinuation and TEAE leading to death are the same participant/event.

[c]1 death during the 8 weeks of safety follow-up after blinded treatment was due to cardiorespiratory arrest in a participant ≥75 years old with a history of cardiac and gastrointestinal disorders and severe CCI score; this event was deemed related to a preexisting condition and unrelated to RBX2660 or the administration procedure.

- Serious AEs were infrequent and none were considered related to RBX2660 or its administration

References

1. Khanna S, et al. *Mayo Clin Proc.* 2012;87(11):1106-1117.
2. DePestel DD, et al. *J Pharm Pract.* 2013;26(5):464-475.
3. Khanna S, et al. *J Intern Med.* 2021;290:294-309.
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.
7. Charlson ME, et al. *J Chronic Dis.* 1987;40(5):373-383.

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 pfeuerstadt@gastrocenter.org.

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