E0100

24-Month Sustained Clinical Response and Safety of RBX2660 in Participants With Recurrent *Clostridioides difficile* Infection: Subgroup Analysis

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BACKGROUND

- *Clostridioides difficile* (*C. difficile*) is an opportunistic pathogen that causes an estimated 500,000 infections per year in the United States[1]
- Microbiota-based treatments have shown promise in reducing recurrent *C. difficile* infection (rCDI)[2]
- RBX2660 is a standardized, microbiota-based live biotherapeutic product being investigated as a treatment option for rCDI[2,3]
- RBX2660 is administered rectally as a single dose, without the need for sedation, colonoscopy, or bowel preparation
- We present a subgroup analysis on the long-term efficacy and safety of RBX2660 in participants with rCDI in PUNCH CD Open-Label (NCT02589847), a prospective, multicenter, open-label, phase 2 trial[3]

METHODS

- PUNCH CD Open-Label participants enrolled were ≥18 years old with either ≥2 episodes of rCDI treated with standard-of-care antibiotic therapy after a primary CDI episode, or ≥2 episodes of severe CDI requiring hospitalization
- Participants were required to have a positive stool test for *C. difficile* toxins A/B or toxin gene expression by nucleic acid amplification within 60 days before enrollment and were on antibiotics to treat CDI at the time of enrollment
- Participants received up to 2 doses of RBX2660 rectally administered 7 ± 2 days apart
- The primary endpoint, treatment success, was defined as the absence of CDI diarrhea without the need for CDI retreatment for 8 weeks after completing study treatment
  - Sustained response was evaluated at 6, 12, and 24 months in participants who experienced treatment success at 8 weeks
- Treatment-emergent adverse events (TEAEs) were defined as events with onset dates on or after the start of study treatment and were collected through 6 months
- Long-term safety data, TEAEs and serious TEAEs were recorded at 6 and 12 months after treatment; events between 12 and 24 months were recorded during the study exit interview and intended to capture serious TEAEs after the last dose of RBX2660
- In this post hoc subgroup analysis, we report the 6-, 12-, and 24-month outcomes of 8-week responders by age, sex, race, and number of prior CDI episodes

RESULTS

- Among the 149 participants treated with RBX2660 in the full analysis set, 91% were White, 64% were female, 58% were ≥65 years of age, and 50% had ≥4 prior episodes of CDI[3]
- 78.9% (112/142) of RBX2660-treated participants had treatment success at 8 weeks[3]
- Sustained response rates were 97% (109/112), 95% (101/106), and 91% (88/97) at 6, 12, and 24 months, respectively[3]

KEY TAKEAWAYS

1 Across demographic subgroups, the majority of RBX2660 responders showed a sustained clinical response, remaining free of CDI recurrence up to 2 years after treatment

2 Long-term safety data reinforce that RBX2660 is well tolerated

3 No evidence of development of new disease associated with RBX2660 with up to 2 years of follow-up

Table 1. Demographics and Baseline Characteristics by Age, Sex, Race, and Number of Prior CDI Episodes (FAS[a])

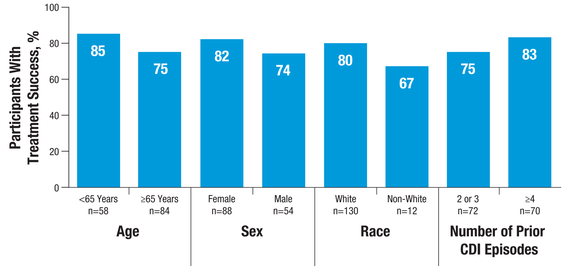
	Age		Sex		Race		Number of Prior CDI Episodes	
	<65 Years (n=62)	≥65 Years (n=87)	Female (n=95)	Male (n=54)	White (n=136)	Non-White (n=13)	2 or 3 (n=74)	≥4 (n=75)
Age, mean (SD), years	46.4 (13.5)	78.4 (8.4)	63.7 (19.6)	67.5 (18.2)	65.0 (19.1)	66.7 (21.1)	63.9 (20.1)	66.3 (18.3)
Age <65 years, n (%)	62 (100.0)	0 (0.0)	46 (48.4)	16 (29.6)	57 (41.9)	5 (38.5)	31 (41.9)	31 (41.3)
Sex (female), n (%)	46 (74.2)	49 (56.3)	95 (100.0)	0 (0.0)	87 (64.0)	8 (61.5)	41 (55.4)	54 (72.0)
Race (White), n (%)	57 (91.9)	79 (90.8)	87 (91.6)	49 (90.7)	136 (100.0)	0 (0.0)	69 (93.2)	67 (89.3)
Number of prior CDI episodes, mean (SD)	3.7 (1.0)	4.0 (1.7)	3.9 (1.4)	3.7 (1.4)	3.7 (1.1)	5.0 (2.9)	2.9 (0.3)	4.8 (1.5)

CDI, *Clostridioides difficile* infection; FAS, full analysis set; N, number of participants; n, number of participants with observation.

[a]The FAS (N=149) includes the RBX2660 safety population, excluding screen failures. The evaluable population (N=142) includes the FAS population that remained evaluable at the primary efficacy end point.

- Across demographic subgroups, treatment success was achieved by 67% to 85% of RBX2660-treated participants
- 83% of participants who had experienced 4 or more prior CDI episodes remained free of CDI recurrence through 8 weeks after RBX2660 treatment

Figure 1. RBX2660 Treatment Success Across Demographic Subgroups (8 Weeks; Evaluable Population)

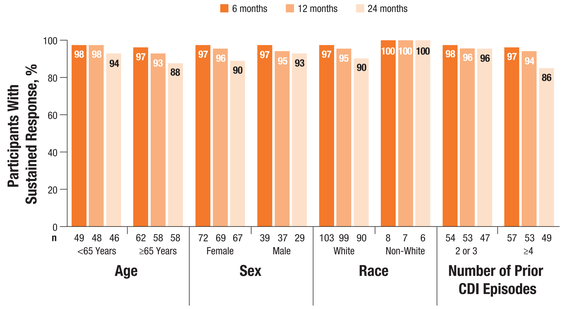


CDI, *Clostridioides difficile* infection.

The evaluable population (N=142) includes the FAS population that remained evaluable at the primary efficacy end point. Success was defined as the absence of CDI diarrhea without the need for retreatment for 8 weeks after completing study treatment.

- Most TEAEs occurred within the first 4 weeks after treatment
- Similar percentages of TEAEs were reported in RBX2660-treated participants across demographic subgroups between 6 and 12 months (range, 31%-43%) and 12 and 24 months (range, 23%-37%) after treatment with RBX2660

Figure 2. Sustained Clinical Response in Patients With 8-Week RBX2660 Treatment Success Across Demographic Subgroups Through 2 Years After RBX2660 Treatment



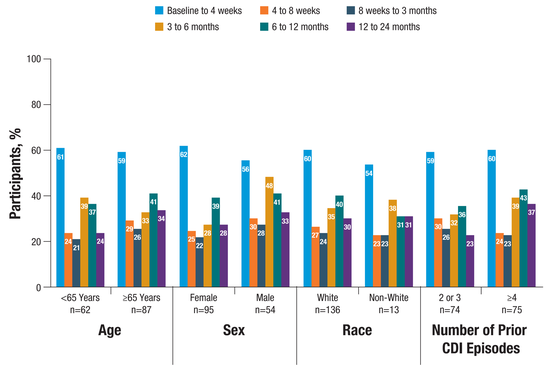
CDI, *Clostridioides difficile* infection.

Numbers at top of the bars are the percentage of participants with sustained response. Numbers below the bars are the total number of assessed participants with follow-up through specified time points.

Between 6 and 24 months, 35 participants discontinued the study (withdrawal by subject [n=10], death [n=16], lost to follow-up [n=5], administrative closure [n=2], site terminated by sponsor [n=1], adverse event [n=1]).

- 98.0%, 97.9%, and 93.5% of participants <65 years of age and 96.8%, 93.1%, and 88.0% of participants ≥65 years of age showed sustained treatment success from week 8 through 6, 12, and 24 months after treatment, respectively
- Similar sustained response rates were demonstrated in participants categorized by sex, race, and number of prior CDI episodes

Figure 3. Summary of TEAEs by Onset Interval Across Demographic Subgroups Through 2 Years After RBX2660 Treatment



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

TEAEs and serious TEAEs were collected at 6 and 12 months of follow-up; events between 12 and 24 months were collected during the study exit interview and intended to capture serious TEAEs after the last dose of RBX2660.

Table 2. Summary of Adverse Events Across Demographic Subgroups Through 2 Years After RBX2660 Treatment

	Participants, n (%)							
	Age		Sex		Race		Number of Prior CDI Episodes	
Severity	<65 Years (n=62)	≥65 Years (n=87)	Female (n=95)	Male (n=54)	White (n=136)	Non-White (n=13)	2 or 3 (n=74)	≥4 (n=75)
Mild	19 (30.6)	12 (13.8)	21 (22.1)	10 (18.5)	30 (22.1)	1 (7.7)	17 (23.0)	14 (18.7)
Moderate	22 (35.5)	27 (31.0)	41 (43.2)	8 (14.8)	43 (31.6)	6 (46.2)	21 (28.4)	28 (37.3)
Severe	7 (11.3)	17 (19.5)	11 (11.6)	13 (24.1)	24 (17.6)	0 (0.0)	11 (14.9)	13 (17.3)
Potentially life-threatening	2 (3.2)	17 (19.5)	8 (8.4)	11 (20.4)	16 (11.8)	3 (23.1)	8 (10.8)	11 (14.7)

Percentages represent the number of participants in the FAS; TEAEs and serious TEAEs were collected at 6 and 12 months of follow-up; events between 12 and 24 months were collected during the study exit interview and intended to capture serious TEAEs after the last dose of RBX2660.

References

1. Guh AY, et al. *N Engl J Med.* 2020;382:1320-1330.
2. Langdon A, et al. *Genome Med.* 2021;13:28.
3. Orenstein R, et al. *BMC Infect Dis.* 2022;22:245.

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