D0099

Efficacy and Safety of RBX2660 in Reducing Recurrent *Clostridioides difficile* Infection in Patients With Underlying Gastrointestinal Comorbidities

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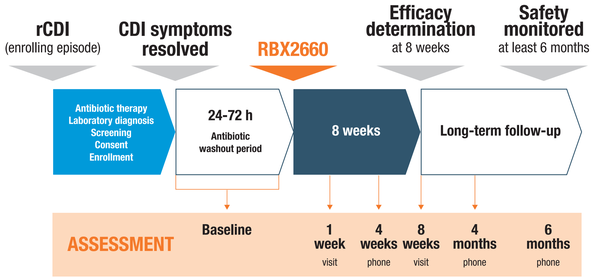
BACKGROUND

- *Clostridioides difficile* infection (CDI) is the most common healthcare-associated infection, affecting ~500,000 people in the United States annually[1,2]
- Several underlying gastrointestinal (GI) comorbidities are known risk factors for recurrent CDI (rCDI), yet patients with GI comorbidities are often excluded from prospective clinical trials[3,4]
- We report the efficacy and safety of RBX2660, a rectally administered, microbiota-based live biotherapeutic, in adult participants categorized by GI comorbidity subgroups from an ad hoc analysis of PUNCH CD3-OLS (NCT03931941), an ongoing open-label phase 3 study

METHODS

- Participants enrolled in PUNCH CD3-OLS were ≥18 years old with medically documented rCDI, including first recurrence patients as determined by the treating physician and assessed with current standard-of-care (SOC) diagnostic methods
- Participants with comorbid conditions unrelated to GI disorders, GI comorbidities, and immunocompromising conditions were identified based on medical history and included in this ad hoc analysis of the modified intent-to-treat (mITT) population
- After SOC antibiotics and a washout period of 24 to 72 hours, participants received a single 150-mL dose of RBX2660 via rectal administration
- Treatment success was defined as remaining free of CDI recurrence for 8 weeks after treatment
- Participants were monitored for recurrence and treatment-emergent adverse events (TEAEs) for at least 6 months after treatment
- Efficacy data are presented for the mITT population, and demographics and safety data are presented for the safety population

Figure 1. PUNCH CD3-OLS Study Design



CDI, *Clostridioides difficile* infection; rCDI, recurrent *Clostridioides difficile* infection.

KEY TAKEAWAYS

1. **RBX2660 treatment success rates at week 8 were comparable for participants with and without GI comorbidities**
2. **Clinical response at week 8 was maintained through 6 months in RBX2660 responders with and without GI comorbidities**
3. **RBX2660 was well tolerated in participants regardless of underlying GI comorbidities**
4. **These results suggest consistent efficacy and safety for RBX2660 in reducing rCDI in a patient population with underlying GI comorbidities**

RESULTS

Table 1. Demographics and Baseline Characteristics by GI Subgroup (safety population, N=483)

	All RBX2660-treated participants (N=483)				
GI comorbidities	**GERD**	**Any history of IBS**	**Any history of diverticulitis**	**IBD**	**Unspecified colitis**
RBX2660-treated participants with GI comorbidity present, % (n)	38.9 (188)	13.2 (64)	20.5 (99)	11.2 (54)	3.5 (17)
Age, median (IQR), years	67.5 (56.0-76.0)	57.5 (40.5-67.5)	71 (63.0-78.0)	48.5 (40.0-66.0)	55 (34.0-64.0)
≥65 years, %	55.9	28.1	70.7	25.9	23.5
Female, % (n)	69.1 (130)	78.1 (50)	71.7 (71)	51.9 (28)	58.8 (10)
Number of CDI episodes before blinded treatment, % (n)					
<3	31.9 (60)	35.9 (23)	35.4 (35)	31.5 (17)	35.3 (6)
≥3	68.0 (128)	64.1 (41)	64.6 (64)	68.5 (37)	64.7 (11)
Charlson Comorbidity Index at screening, %					
<3	49.5	64.1	29.3	66.7	82.4
≥3	50.3	35.9	70.7	33.3	17.6

CDI, *Clostridioides difficile* infection; GERD, gastroesophageal reflux disease; GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

Participants could have more than 1 comorbidity; type of IBS was not differentiated in this population; IBD included ulcerative colitis and Crohn's disease, and unspecified colitis included indeterminate colitis, pancolitis, and undefined colitis; diverticulitis was exclusionary if antibiotics were required at the time of screening or if the participant had surgical intervention within 6 months of enrollment or planned within 8 months of enrollment.

- **GI comorbidities present in RBX2660-treated participants included GERD, IBS, diverticulitis, IBD, and unspecified colitis**

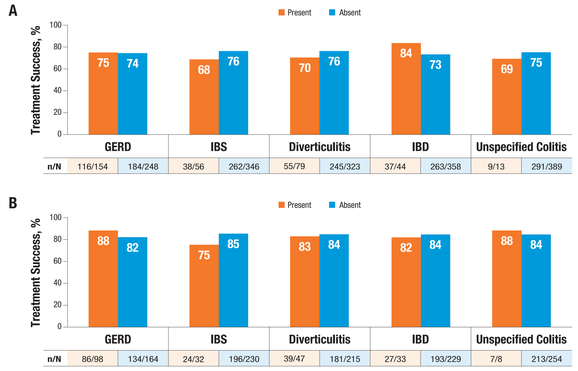
8-Week Treatment Success

- 75% (300/402) of RBX2660-treated participants had treatment success at week 8 (**Figure 2A**)
- Treatment success rates for participants in the IBD group were slightly higher compared with participants without IBD and were otherwise comparable across the remaining groups. These trends will be reassessed at the time of the final analysis

6-Month Sustained Response

- RBX2660 successfully sustained clinical response through 6 months across GI comorbidity subgroups (**Figure 2B**)
- 84% (220/262) of the RBX2660 treatment responders at week 8 with adjudicated outcomes remained recurrence-free through 6 months
- 60% (157/262) of the RBX2660 treatment responders had ≥1 GI comorbidity, and 105 participants had none
- 84% (132/157) of the RBX2660 treatment responders with ≥1 GI comorbidity remained recurrence-free through 6 months

Figure 2. 8-Week Treatment Success and 6-Month Sustained Response in Participants With and Without GI Comorbidities



GERD, gastroesophageal reflux disease; GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; mITT, modified intent-to-treat; Present, GI comorbidity present; Absent, GI comorbidity absent.

Participants could have ≥1 comorbidity.

Treatment success at week 8, only participants with adjudicated treatment outcomes are included (N=402 of 469 screened participants in the mITT population treated with RBX2660); sustained treatment response adjudicated results through 6 months, were available for 262 of 300 participants in the mITT population with treatment success at week 8.

Safety

- Overall, TEAEs were similar between participants with and without GI comorbidities (**Table 2**)

- **Most TEAEs were mild to moderate in severity**
- **Potentially life-threatening TEAEs and TEAEs leading to discontinuation were infrequently reported**
- **3 deaths (0.6%) were reported following TEAEs of cardiac arrest, pneumosepsis, and spina bifida**
- **None of the TEAEs that led to death were attributed to RBX2660 or the procedure and all were attributed to preexisting conditions and/or *C. difficile* disease**

Table 2. Overall Summary of Adverse Events by GI Subgroup (safety population, N=483)

	All RBX2660-treated participants									
	GERD		IBS		Diverticulitis		IBD		Unspecified colitis	
Presence or absence of GI comorbidities	Present n=188	Absent n=295	Present n=64	Absent n=419	Present n=99	Absent n=384	Present n=54	Absent n=429	Present n=17	Absent n=466
All TEAEs, % (n)	53.2 (100)	50.2 (148)	64.1 (41)	49.4 (207)	47.5 (47)	52.3 (201)	46.3 (25)	52.0 (223)	52.9 (9)	51.3 (239)
Mild TEAEs, % (n)[a]	13.3 (25)	20.0 (59)	17.2 (11)	17.4 (73)	13.1 (13)	18.5 (71)	13.0 (7)	17.9 (77)	17.6 (3)	17.4 (81)
Moderate TEAEs, % (n)[a]	26.6 (50)	20.3 (60)	31.3 (20)	21.5 (90)	23.2 (23)	22.7 (87)	18.5 (10)	23.3 (100)	23.5 (4)	22.7 (106)
Severe TEAEs, % (n)[a]	11.2 (21)	8.8 (26)	14.1 (9)	9.1 (38)	9.1 (9)	9.9 (38)	14.8 (8)	9.1 (39)	11.8 (2)	9.7 (45)
Potentially life-threatening, % (n)[a]	2.1 (4)	1.0 (3)	1.6 (1)	1.4 (6)	2.0 (2)	1.3 (5)	0 (0)	1.6 (7)	0 (0)	1.5 (7)
TEAEs related to investigational product, % (n)	15.4 (29)	15.3 (45)	20.3 (13)	14.6 (61)	11.1 (11)	16.4 (63)	9.3 (5)	16.1 (69)	17.6 (3)	15.2 (71)
TEAEs related to enema procedure, % (n)	8.5 (16)	6.4 (19)	7.8 (5)	7.2 (30)	3.0 (3)	8.3 (32)	5.6 (3)	7.5 (32)	5.9 (1)	7.3 (34)

GERD, gastroesophageal reflux disease; GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; TEAE, treatment-emergent adverse event.

[a]Counted in maximum severity. Missing severity is counted as maximum severity (ie, potentially life-threatening).

- **RBX2660 reduced rCDI across GI comorbidity subgroups at week 8**
- **RBX2660 responders at 8 weeks with and without GI comorbidities showed a sustained clinical response at 6 months**

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