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Health-Related Quality of Life in Patients with One Prior Episode of Recurrent *Clostridioides Difficile* Infection (rCDI): Results from the RBX2660 Phase 3 Randomized, Placebo-Controlled rCDI Trial (PUNCH CD3)

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INTRODUCTION

- *Clostridioides difficile* infection (CDI) is the most frequently identified healthcare associated infection (HAI) in the US with approximately 500,000 incident cases per year[1,2]
- CDI occurs through ingestion of spores followed by colonization of the colon and production of toxins, causing a range of symptoms including diarrhea, colonic perforation, and death[3-4]
- Standard treatment involving antibiotics often fails to achieve a lasting cure for CDI; up to 35% of patients treated for an initial case of CDI recur and up to 65% of patients with multiple recurrences experience recurrent CDI (rCDI)[5-8]
- RBX2660 is an investigational live biotherapeutic product developed to reduce recurrence of CDI. PUNCH CD3, a RBX2660 phase 3 randomized placebo (PBO) controlled trial (NCT03244644), included patients with at least one prior rCDI episode and at least one round of standard-of-care oral antibiotic therapy, or with at least two episodes of severe CDI resulting in hospitalization within the prior year
- Here we report post-hoc analyses of health-related quality of life (HRQL) within an 8-week blinded period for a subgroup of patients in the PUNCH CD3 trial who had first recurrence. HRQL was measured using the *Clostridioides difficile* Health-related Quality-of-Life Questionnaire (Cdiff32), a disease-specific instrument

OBJECTIVE

- Summarize Cdiff32 total and domain-specific (physical, mental, social) scores at baseline and week 8 separately for patients randomized to RBX2660 or PBO among patients with one prior rCDI episode
- Compare differences in change from baseline to week 8 in Cdiff32 total and domain scores between patients randomized to RBX2660 and to PBO among patients with one prior rCDI episode

METHODS

- The analysis included adult patients with one prior rCDI episode from the phase 3 PUNCH CD3 trial's modified intention-to-treat (mITT) population. The mITT population was defined as all randomized subjects who successfully received blinded treatment but excluding: subjects who withdrew prior to treatment; subjects in whom treatment was attempted but not completed; and subjects who discontinued from the study prior to evaluation of Treatment Failure/Success for the primary endpoint if the reason for exit was not related to CDI symptoms. Patients were required to have a Cdiff32 assessment at baseline and week 8
- The disease-specific Cdiff32 comprises three domains (physical, mental, social) and a total score; scores range from 0–100 (100 best possible)
- Absolute scores for the total and domain scores were summarized via mean and standard deviation at baseline and week 8 by treatment arm. The differences in change from baseline to week 8 were summarized via mean and standard deviation, and comparisons between treatment arms were conducted using Wilcoxon rank-sum tests
- Adjusted analyses were conducted to compare between-treatment week 8 Cdiff32 scores (total and domains), controlling for the corresponding baseline Cdiff32 score, treatment (RBX2660 or PBO), sex (male vs. female), age (years), prior fidaxomicin use, prior proton pump inhibitor use, and common comorbidities (metabolism and nutrition disorders, surgical and medical procedures, infections and infestations, gastrointestinal disorders, and psychiatric disorders)
- Per trial protocol, patients experiencing recurrence after blinded treatment received open-label RBX2660 per physician discretion; these participants were excluded. As-observed data were used for all analyses

KEY TAKEAWAYS

1. **No prior research has reported HRQL impact of an investigational live biotherapeutic product in rCDI patients with 1 prior rCDI (first recurrence)**
2. **Our findings demonstrated significant improvements in HRQL for RBX2660-treated patients compared to PBO-treated patients in this subgroup of patients**
3. **Future research is needed to further validate the HRQOL benefits of RBX2660 in treating first recurrent CDI patients**

RESULTS

Table 1. Baseline characteristics

	RBX2660 (N=43) Mean ± SD / N (%)	Placebo (N=23) Mean ± SD / N (%)
Demographics		
Age (years)	56.8 ± 19.0	59.1 ± 16.7
Sex		
Female	27 (62.8)	16 (69.6)
Male	16 (37.2)	7 (30.4)
Race		
American Indian or Alaska Native	0 (0.0)	0 (0.0)
Asian	0 (0.0)	0 (0.0)
Black or African American	4 (9.3)	0 (0.0)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)
Multiple	0 (0.0)	0 (0.0)
White	39 (90.7)	21 (91.3)
Other	0 (0.0)	2 (8.7)
Disease characteristics		
Duration of prior CDI episode (days)	26.7 ± 14.3	24.2 ± 9.2
Antibiotics used at screening		
Other	3 (7.0)	0 (0.0)
Vancomycin	36 (83.7)	21 (91.3)
Fidaxomicin	4 (9.3)	2 (8.7)
Vancomycin duration on recent CDI (days)	18.6 ± 14.0	17.2 ± 9.9
Prior hospitalization due to CDI	7 (16.3)	4 (17.4)
Proton pump inhibitor use	8 (18.6)	8 (34.8)
Surgical and medical procedures	24 (55.8)	11 (47.8)
Infections and infestations	23 (53.5)	13 (56.5)
Gastrointestinal disorders	25 (58.1)	11 (47.8)
Psychiatric disorders	25 (58.1)	10 (43.5)
Metabolism and nutrition disorders	24 (55.8)	10 (43.5)

[a] Includes patients from the mITT population with both baseline and week 8 Cdiff32 assessments.

Table 2. Cdiff32 component scores at baseline and week 8 by treatment arm

	Baseline score		Week 8 score			
Component (Mean ± SD)	**RBX2660**	**Placebo**	**RBX2660**	**Placebo**	**Difference-in-difference**	**Unadjusted P-value**
Total	40.7 ± 15.7	47.3 ± 20.8	75.9 ± 18.6	69.0 ± 23.4	13.5 ± 5.7	< 0.05 *
Physical	47.3 ± 19.4	51.7 ± 22.2	84.2 ± 16.9	76.6 ± 24.1	11.9 ± 6.1	0.07
Mental	31.7 ± 15.0	40.8 ± 21.8	66.5 ± 22.2	59.4 ± 25.3	16.2 ± 6.0	< 0.01 *
Social	51.6 ± 22.0	54.6 ± 26.3	80.4 ± 21.8	75.8 ± 24.7	7.6 ± 7.4	0.45

[a] Statistical comparisons between treatment arms were performed using the Wilcoxon rank-sum tests.

Table 3. Multivariable adjusted analyses of Cdiff32 total and domain scores at week 8[a]

Component	Estimate[b] (95% CI)	P-value
Total score	11.0 (1.3, 20.7)	<0.05 *
Physical domain	10.7 (1.4, 20.1)	<0.05 *
Mental domain	13.1 (2.0, 24.1)	<0.05 *
Social domain	7.0 (-3.8, 17.9)	0.21

CI = confidence interval.

[a] The adjusted analyses controlled for baseline Cdiff32 score, treatment (RBX2660 or PBO), sex, age (years), prior fidaxomicin use, prior proton pump inhibitor use, and common comorbidities (metabolism and nutrition disorders, surgical and medical procedures, infections and infestations, gastrointestinal disorders, and psychiatric disorders).

[b] The estimate from the regression reflects the adjusted difference-in-difference comparing RBX2660 change from baseline vs. placebo change from baseline.

- **Adjusted analyses showed statistically significant differences (all p<0.05) favoring RBX2660 over PBO at week 8 for the total score (11.0, 95% confidence interval: [1.3; 20.7]), physical domain (10.7, [1.4; 20.1]) and mental domain (13.1, [2.0; 24.1])**

- **Unadjusted analyses showed statistically significantly greater HRQL improvements with RBX2660 vs PBO at week 8 for the total score (difference-in-difference: 13.5 ± 5.7, p<0.05) and mental domain (16.2 ± 6.0, p<0.01)**
- **Numerically but not statistically significant improvements were observed for the physical domain (11.9 ± 6.1, p=0.07) and the social domain (7.6 ± 7.4, p=0.45)**

- **Out of 262 patients enrolled in PUNCH CD3, a total of 86 patients (53 RBX2660, 33 PBO) had 1 prior rCDI episode (33% of all trial patients)**
- **Among these 86 patients, 66 (76.7%) had Cdiff32 data at both baseline and week 8 (43 RBX2660, 23 PBO)**
- **These patients were aged (mean ± SD) 56.8 years ± 19.0 in the RBX2660 arm and 59.1 years ± 16.7 in the PBO arm, and 62.8% and 69.6% were female in the RBX2660 and PBO arms, respectively**

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