Poster P2570

Real-World Experience with Microbiota Treatment for the Prevention of Recurrent *Clostridioides difficile* Infection

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Key Findings

- **RBL was effective in preventing recurrence at 8 weeks with the large majority of patients experiencing sustained response at 6 months.**
- **Among those with rCDI risk factors, recurrence was most commonly seen in patients ≥ 65 years of age.**
- **Recurrence was most frequent at week 4 following treatment.**
- **RBL was safe and well tolerated.**
- **Results are comparable to the data reported in the PUNCH CD3 trial despite a more comorbid population.[2,3]**

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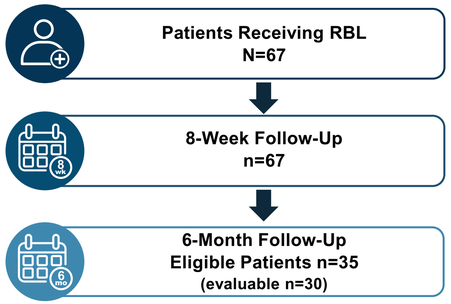
Introduction

- Fecal microbiota, live-jslm (RBL) is the first-in-class microbiome-based therapy approved by the FDA in November 2022 for the prevention of recurrence of *Clostridioides difficile* infection (rCDI) in adults.
- This rectally-administered, pre-packaged single dose has been proven to be safe and efficacious in clinical trials.
- The Bayesian analysis from the PUNCH CD3 clinical trial showed treatment success at 8 weeks of 70.6% with RBL vs 57.5% with placebo.
- The objective of this study is to report the effectiveness of RBL in an outpatient real-world setting.

Methods

- A retrospective, multicenter, single-arm cohort study was conducted of patients ≥18 years old who received RBL in Infectious Disease or Gastroenterology physician offices across the US between February 2023 to May 2024.
- Medical records were reviewed for data including patient demographics, comorbidities, number of prior CDI episodes, prior CDI treatment, rCDI risk factors, and CDI treatment for current episode, including standard of care (SoC) antibiotics.
- Utilization characteristics included diagnostic testing method to confirm CDI, SoC antibiotic use for current CDI episode, including duration of use, and time from SoC completion of RBL administration.
- rCDI risk factors assessed included age ≥65 years, use of gastric acid suppressant therapy, non-CDI antibiotic use within 4 weeks prior to current CDI episode, and a compromised immune system.
- Other factors contributing to rCDI were assessed including inflammatory bowel disease, CDI with severe presentation, or chronic renal disease.
- Gastrointestinal adverse events related to RBL administration were collected.
- Recurrence was defined as any occurrence of diarrhea with 3 liquid bowel movements or more within 24 hours and was assessed at 8 weeks and 6 months post-RBL administration.
- Treatment success was defined as absence of recurrence within 8 weeks, and sustained response was defined as continued absence of recurrence through 6 months.
- Continuous data were reported as means with standard deviations (SD) or medians with interquartile ranges (IQR), and categorical data as counts and percentages. Risk factors for rCDI post-RBL administration were calculated with two-tailed Fishers Exact test or Wilcoxon Rank Sum test.

Study Design

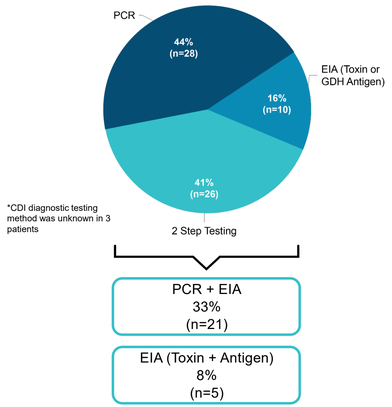


Patient Characteristics

Characteristic	Results (N=67)
Age, median (IQR) years	74 (63-81.5)
Female, n (%)	47 (70.1)
Hospitalization within 4 weeks of current CDI, n (%)	4 (6.0)
Charlson comorbidity index, median (IQR)	4 (3-6.5)
CDI history	
Number of prior CDI episodes, not including current, median (IQR)	3 (1-3)
0 episodes	2 (3.0)
1 episode, n (%)	17 (25.4)
2 episodes, n (%)	14 (20.9)
≥3 episodes, n (%)	34 (50.7)
Number of rCDI risk factors, n (%)	
0	6 (9.0)
1	24 (35.8)
2	22 (32.8)
≥3	15 (22.4)
rCDI risk factors, n (%)	
Age ≥65 years	48 (71.6)
Concurrent gastric acid suppressant use[a]	37 (55.2)
Immunocompromised[b]	16 (23.9)
Non-CDI antibiotic use within 4 weeks prior to current CDI	14 (20.9)
Other characteristics, n (%)	
Inflammatory bowel disease	5 (7.5)
Crohn's Disease	2 (3.0)
Ulcerative Colitis	3 (4.5)
Current CDI with severe presentation[c]	8 (11.9)
Chronic renal disease	10 (14.9)
Bezlotoxumab therapy with prior episode	9 (13.4)

Diagnosis and Treatment Characteristics

Diagnostic Method for *C. difficile*

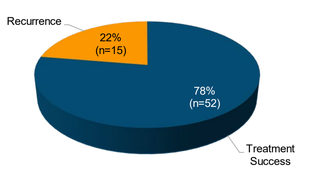


Treatment Characteristics

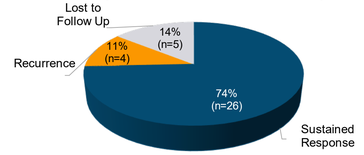
Treatment Characteristics	Results (N=67)	
Standard of care antibiotic treatment	**n (%)**	**Duration of therapy, median days (IQR)**
Fidaxomicin	30 (44.8)	10 (10-16.8)
Fidaxomicin + vancomycin fixed-dose	5 (7.5)	27 (24-32)
Fidaxomicin + vancomycin taper	2 (3.0)	59 (55-63)
Fidaxomicin + metronidazole	1 (1.5)	17
Vancomycin fixed-dose	21 (31.3)	18 (14-24)
Vancomycin taper	7 (10.4)	47 (43.5-71.5)
Vancomycin taper + metronidazole	1 (1.5)	39
Additional rCDI-related treatment	**n (%)**	
Bezlotoxumab, n (%)	8 (11.9)	
Days to RBL treatment	**median (IQR)**	
Days from SoC completion to RBL	2 (1-4)	
Days from *C. difficile* stool test to RBL	35 (23-65)	
RBL GI AEs	**n (%)**	
Minor leakage	5 (7.5)	

Treatment Success

Treatment Success Rate at 8 Weeks (n=67)

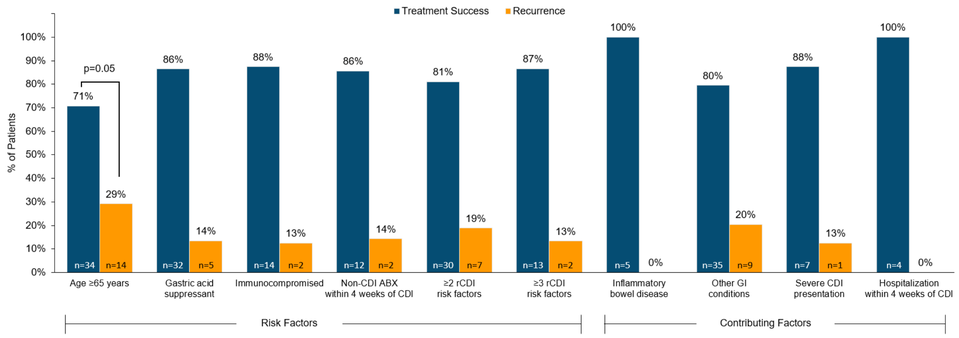


Sustained Response Rate at 6 Months (n=35)



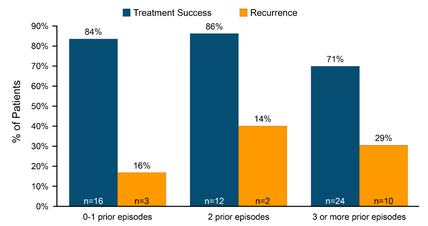
- In the evaluable population (n=30)[d], the sustained response was **87%**.

Analysis of Risk Factors and Contributing Factors at 8 Weeks



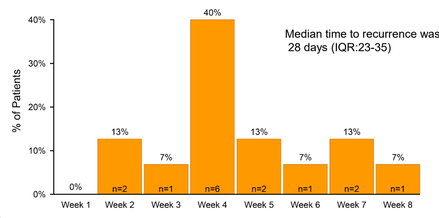
Recurrence Details

Recurrence at 8 weeks by Number of Episodes



- Although not statistically significant, recurrence was highest in patients with 3 or more prior CDI episodes.

Distribution of Recurrences over 8 Weeks



DISCUSSION

This study provides real-world data on the effectiveness of RBL in preventing rCDI in an outpatient setting.

- Over 90% of patients had 1 or more rCDI risk factor, with age ≥65 years being most common.
- Half of patients had ≥3 prior CDI episodes.
- Treatment success was observed in 78% of patients at 8 weeks.
- Sustained response was 87% at 6 months in the evaluable population.
- Among rCDI risk factors, age ≥65 years was associated with a significantly higher incidence of recurrence.
- There were no recurrences in patients with IBD at 8 weeks or at 6 months.
- Although not statistically significant, those with ≤1 recurrence of CDI had treatment success of 84.2%, higher than those with ≥2 or ≥3 recurrences.
- For those with recurrence, most patients experienced recurrence at 4 weeks after receiving RBL.
- RBL administration was safe.
- Limitations of the study include lack of testing to confirm rCDI following RBL administration, potentially leading to higher reported cases of recurrences.

Abbreviations and Definitions

Abbreviations: ABX, antibiotic; AEs, adverse events; CDI, *Clostridioides difficile* infection; EIA, enzyme immunoassay; FMT, fecal microbiota transplant; GDH, glutamate dehydrogenase; GI, gastrointestinal; IQR, interquartile range; LTF, lost to follow up; PCR, polymerase chain reaction; RBL, fecal microbiota, live-jslm; rCDI, recurrent *Clostridioides difficile* infection; SD, standard deviation; SoC, standard of care

Definitions: [a]Proton pump inhibitor and/or histamine-2 receptor antagonist

[b]Due to immunosuppressive medication or underlying disease (immune deficiency, solid organ or hematopoietic stem cell transplant, absolute neutrophil cell count <500 cells/mL)

[c]Defined by any of the following: albumin ≤3.0 g/dl, serum creatinine ≥1.5 times above baseline, hypotension or shock, intensive care unit stay related to CDI, ileus, serum lactate >5 mmol/L, toxic megacolon or colectomy related to CDI, white blood cell count ≥15,000 cells/mL.

[d]6-Month Follow-Up: Non-evaluable patients included lost to follow up (n=3) and expired (n=2)

References

1. Rebyota (fecal microbiota, live - jslm) [package insert]. Roseville, MN: Ferring Pharmaceuticals; 2022.
2. Dubberke ER, et al. Infect Dis Ther. 2023; 12:703–710.
3. Khanna S, et al. Drugs. 2022; 82:1527–1538.

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