Poster P-220

Real-World Effectiveness of Fecal Microbiota, live-jslm for the Prevention of Recurrent *Clostridioides* difficile Infection

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Key Findings

- RBL demonstrated high efficacy at 8
 weeks with the large majority of
 patients recurrence free at 6 months.
- Recurrence was most commonly seen in the first month 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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Background

- Fecal microbiota, live-jslm (RBL) is a live biotherapeutic product 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.
- In the PUNCH CD3 clinical trial, 70.6% of patients achieved treatment success at 8 weeks 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 March 2024.
- Medical records were reviewed for data including patient demographics, comorbidities, number of prior CDI episodes, prior CDI treatment, rCDI risk factors, CDI treatment for current episode, including standard of care (SoC) antibiotics, and adverse events associated with administration of RBL.
- 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 chronic renal disease, CDI with severe presentation or inflammatory bowel disease.

EIA (Toxin + Antigen)

- 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 to RBL administration.
- Patients were evaluated for recurrence of rCDI at 8 weeks and 6 months post-RBL administration as per a standardized clinical protocol.
- Recurrence was defined as 3 or more liquid bowel movements within 24 hours that required CDI-related therapy.
- 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.

Patients Receiving RBL 8-Week Recurrence Follow-Up 6-Month Recurrence Follow-Up

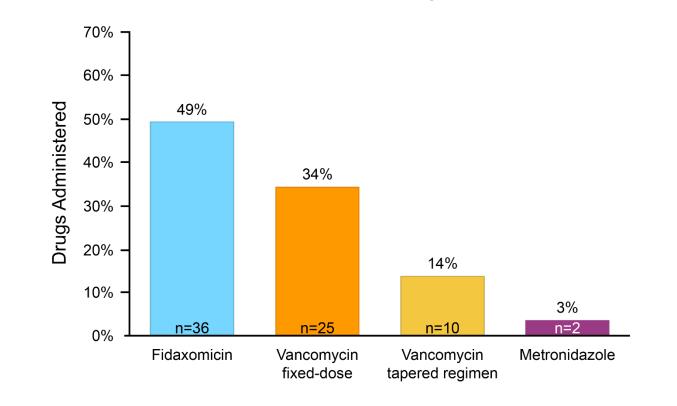
Patient Characteristics

Characteristic	Results (N=64)
Age, median (IQR) years	75 (64.8-82.3)
Female, n (%)	42 (65.6)
Hospitalization within 4 weeks of current CDI, n (%)	4 (6.3)
Charlson comorbidity index, median (IQR)	4.5 (3.0-7.0)
CDI history	
Number of prior CDI episodes, not including current, median (IQR)	3 (1-3)
0 episodes	1 (1.6)
1 episode	19 (29.7)
2 episodes, n (%)	10 (15.6)
≥3 episodes, n (%)	34 (53.1)
Number of rCDI risk factors, n (%)	
0	5 (7.8)
1	21 (32.8)
2	22 (34.4)
≥3	16 (25.0)
rCDI risk factors, n (%)	
Age ≥65 years	48 (75.0)
Concurrent gastric acid suppressant use ^a	38 (59.4)
Immunocompromised ^b	16 (25.0)
Non-CDI antibiotic use within 4 weeks prior to current CDI	13 (20.3)
Other characteristics, n (%)	
Chronic renal disease	11 (17.2)
Current CDI with severe presentation ^c	7 (10.9)
Inflammatory bowel disease	6 (9.4)
Bezlotoxumab therapy with prior episode	8 (12.5)
Bezlotoxumab therapy with current episode	7 (10.9)

Diagnostic Method for C. difficile EIA (Toxin or GDH Antigen) 15% (n=9) 2 Step Testing 41% (n=25) EIA (Toxin or GDH Antigen)

CDI diagnostic testing method was unknown in 3 patients

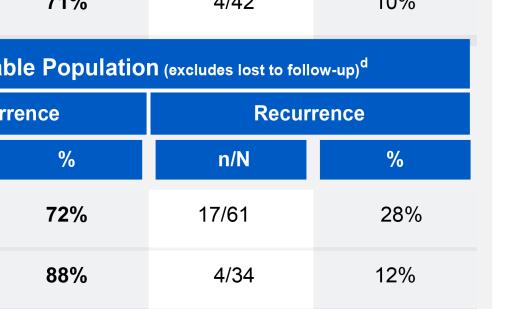
Use of SoC Antibiotics for Current CDI Episode

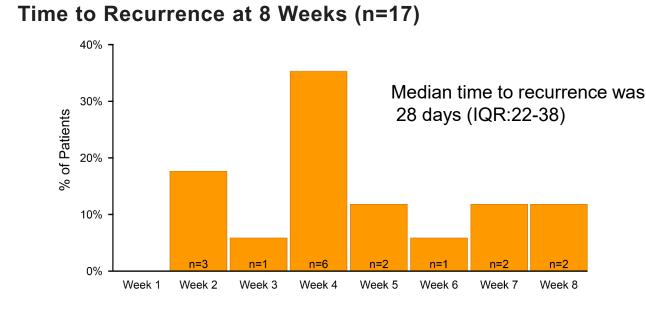


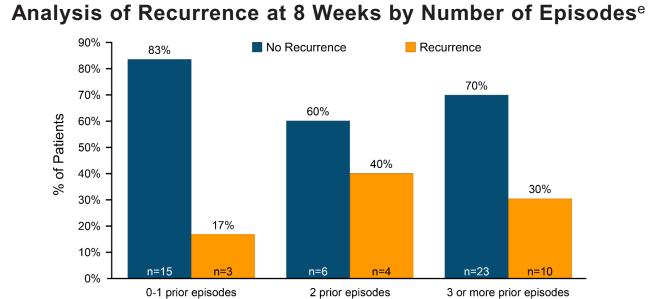
- 73 SoC antibiotics were administered in 64 patients
- 9 patients received 2 SoC antibiotics
- Median durations of SoC therapy were:
 fidaxomicin: 10 days (IQR: 10-17)
- vancomycin fixed-dose: 18 days (IQR: 14-30)
- vancomycin taper: 48 days (IQR: 42.8-72.5)
- metronidazole: 15.5 days (IQR: 12.8-18.3)
- **RBL** Utilization

RBL Utilization	Results
RBL Utilization, median days (IQR)	•
Days from SoC completion to RBL	2 (1-4)
Days from C. difficile stool test to RBL	36 (25-68)
Adverse Events, n (%)	
Minor leakage	4 (6.2)

Recurrence

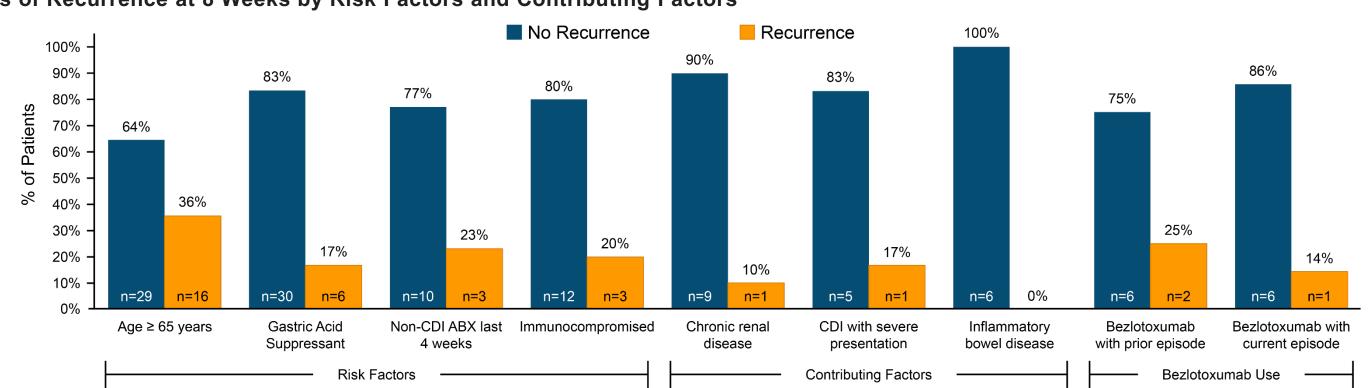






Although not statistically significant, recurrence was lowest in patients with 0-1 prior episodes

Analysis of Recurrence at 8 Weeks by Risk Factors and Contributing Factors^e



• A median time from completion of SoC to RBL of 3 days was associated with a lower risk of recurrence versus 2 days. (data not shown)

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.

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- More than half of patients had ≥3 prior CDI episodes.
- Among those with evaluable data, treatment success was observed in 72% of patients, with sustained response of 88% at 6 months.
- administration.

The highest number of recurrences occurred at 4 weeks post-RBL

- The adverse event rate was low with only minor leakage reported in 4 patients.
- 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; CDI, Clostridioides difficile infection; EIA, enzyme immunoassay; FMT, fecal microbiota transplant; GDH, glutamate dehydrogenase; IQR, interquartile range; PCR, polymerase chain reaction; RBL, fecal microbiota, live-jslm; rCDI, recurrent Clostridioides difficile infection; SD, standard deviation; SoC, standard of care

Definitions: aProton pump inhibitor and/or histamine-2 receptor antagonist; bDue to immunosuppressive medication or underlying disease (immune deficiency, solid organ or hematopoietic stem cell transplant, absolute neutrophil cell count <500 cells/mL); beginned 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; delated to CDI (n=2); 6-Month Follow-Up: Non-evaluable patients included lost to follow up (n=4), deceased unrelated to CDI (n=4); eResults shown for the evaluable population.

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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