PUBLICATION SUMMARY

Developed under the Scientific Information on Unapproved Uses of Approved Medical Products. REBYOTA® (fecal microbiota, live-jslm) has not been approved by the FDA for administration via colonoscopy and the safety and effectiveness of REBYOTA administered via colonoscopy have not been established.

REBYOTA is approved for rectal administration only.

APPROVED INDICATION

REBYOTA (fecal microbiota, live - jslm) is indicated for the prevention of recurrence of *Clostridioides difficile* infection (CDI) in individuals 18 years of age and older, following antibiotic treatment for recurrent CDI.

Limitation of Use

REBYOTA is not indicated for treatment of CDI.

Contraindications

Do not administer REBYOTA to individuals with a history of a severe allergic reaction (eg, anaphylaxis) to any of the known product components.

REBYOTA®
(FECAL MICROBIOTA, LIVE-JSLM)

ADMINISTRATION VIA COLONOSCOPY

Safety and effectiveness of fecal microbiota, live-jslm (REBYOTA®) administered by colonoscopy for prevention of recurrent *Clostridioides difficile* infection: 8-week results from CDI-SCOPE, a single-arm, phase 3b trial

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This publication was supported by Ferring Pharmaceuticals Inc.

[a]Served as investigators in the CDI-SCOPE study, which was funded by Ferring Pharmaceuticals Inc.
[b]Full-time employees at Ferring Pharmaceuticals Inc.

FERRING PHARMACEUTICALS

Microbiome Therapeutics Development

ADMINISTRATION VIA COLONOSCOPY IN A US-BASED MULTICENTER SINGLE-ARM TRIAL

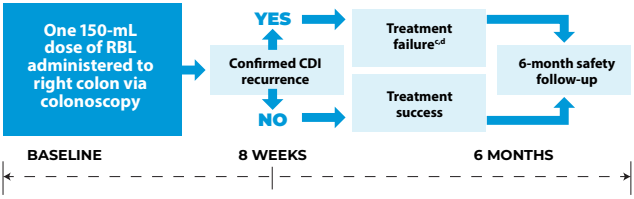
STUDY DESIGN

- CDI-SCOPE was a single-arm, exploratory, phase 3b trial conducted at 12 sites in the United States that assessed the safety and clinical effectiveness of fecal microbiota, live-jslm (REBYOTA®, abbreviated here as RBL) when administered by colonoscopy to adults with rCDI

CDI-SCOPE Study Design[a]

N=41[b]

- Aged ≥18 years
- Documented rCDI
- Completed ≥10 consecutive days and ≤60 days of antibiotic treatment
- Controlled CDI diarrhea for ≥2 consecutive days
- 24-72 hours antibiotic washout period
- Completed bowel preparation



PRIMARY ENDPOINT

- RBL-related TEAEs after RBL administration through 8 weeks or to confirmed treatment failure[d]

SECONDARY ENDPOINTS

- Treatment success (absence of CDI recurrence for 8 weeks following RBL administration)
- Physician experience administering RBL via colonoscopy, and physician perception of patient benefit

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CDI, *Clostridioides difficile* infection; RBL, fecal microbiota, live-jslm; rCDI, recurrent CDI; TEAEs, treatment-emergent adverse events.

[a]Follow-up visits occurred at 1, 2, 4, and 8 weeks, and 3 and 6 months after administration.

[b]Of 54 participants screened between May 2023 and June 2024, 41 were enrolled and received RBL via colonoscopy; 39 participants finished the 8-week visit and 2 withdrew prior to Week 8. Participants were mostly White (95.1%) and female (87.8%), having a mean (SD) age of 61.2 (14.9) years and mean (SD) body mass index of 26.3 (4.8). Among enrolled participants, the mean (SD) number of previous CDI episodes was 3.2 (1.8), with mean (SD) duration of the last CDI episode of 24.2 (11.1) days. Most commonly prescribed antibiotics during participants' most recent CDI episode were vancomycin (n=29; 63.0%) and fidaxomicin (n=16; 34.8%). Most participants were not hospitalized due to their last CDI episode (n=38; 92.7%).

[c]Participants who experienced CDI recurrence within 8 weeks and 6 months were diagnosed and treated according to standard of care at the investigator's discretion.

[d]Treatment failure (i.e., recurrence) was defined as the presence of CDI diarrhea and a positive test for *C. difficile* toxin (per the site's standard practice) within 8 weeks after RBL administration, while treatment success was defined as absence of CDI diarrhea for 8 weeks after RBL administration.

PARTICIPANT ELIGIBILITY AND SCREENING

- Adults (aged ≥18 years) with a diagnosis of rCDI (≥1 recurrence or ≥2 episodes and a positive stool test for *C. difficile* toxin or toxigenic *C. difficile*), a current prescription for antibiotics to control CDI-related diarrhea, and who were a candidate for colonoscopy were eligible for screening
- Completed standard-of-care antibiotic therapy a minimum of 10 consecutive days but not more than 60 total days before 24- to 72-hour washout prior to bowel prep and RBL administration via colonoscopy
- CDI symptoms must have been under control prior to and during the antibiotic washout period, as recorded by participants in an electronic stool diary

INELIGIBLE PARTICIPANTS

- Participants were ineligible if:
  - they were using systemic antibiotics for an indication other than rCDI,
  - had symptoms caused by a confirmed intestinal pathogen other than *C. difficile*,
  - had current uncontrolled diarrhea unrelated to CDI,
  - had CDI unresponsive to antibiotic therapy,
  - had active/fulminant colitis,
  - or had received any microbiota-based therapies (e.g., fecal microbiota transplantation [FMT], RBL) within 6 months before screening or between screening and baseline.

RBL ADMINISTRATION

- Following the antibiotic washout period, bowel preparation for colonoscopy was conducted using a method determined at the investigator's discretion
- All eligible participants received one administration of 150-mL RBL dose via colonoscopy to the right side of the colon, i.e., between the ileocecal valve and the hepatic flexure of the colon

STUDY LIMITATIONS

- The trial was a single-arm open-label design, which introduces the potential for bias in both treatment administration and outcome assessment. The absence of a control group limits the ability to draw definitive conclusions regarding the comparative efficacy of RBL relative to other available treatments
- Sample size was small and the trial population was somewhat homogenous in terms of sex and race, which restrict the generalizability of the results and potentially the broader applicability of RBL in diverse patient populations
- Relatedness of treatment-emergent adverse events (TEAEs) was limited to their potential association with RBL, and potential associations with other variables such as preexisting conditions were not captured
- RBL was not used for the treatment of active CDI, including fulminant disease as well as antibiotic-refractory CDI
- The absence of formal statistical hypothesis testing and procedural variability with regard to colonoscopy administration limit the ability to draw definitive conclusions regarding the clinical effectiveness of RBL

ADMINISTRATION VIA COLONOSCOPY
RESULTS FROM A US-BASED MULTICENTER SINGLE-ARM TRIAL

PRIMARY ENDPOINT: SAFETY

5 TEAEs (n=4, 9.8%) were reported, all of which were gastrointestinal disorders and mild in severity

TEAEs assessed as related to RBL occurring within 8 weeks of RBL administration

System organ class	RBL (N=41)	
Preferred term	Participants, n (%)	Number of events
Adverse events related to RBL	4 (9.8)	5
Gastrointestinal disorders	4 (9.8)	5
Abdominal distension	2 (4.9)	2
Constipation	1 (2.4)	1
Diarrhea	1 (2.4)	1
Flatulence	1 (2.4)	1

Overall, 33 TEAEs occurred in 18 (43.9%) participants within 8 weeks, most of which were mild (25/33; 75.8%) or moderate (5/33; 15.2%) in severity

- 2 participants (4.9%) experienced serious TEAEs, considered unrelated to RBL
- No TEAEs leading to death or intensive care unit admission reported within 8 weeks

Safety summary of TEAEs occurring through 8 weeks after RBL administration

	RBL (N=41)	
	Participants, n (%)	Number of events
TEAEs	18 (43.9)	33
Mild	14 (34.1)	25
Moderate	3 (7.3)	5
Severe	2 (4.9)	2
Potentially life-threatening	1 (2.4)[a]	1
Serious TEAEs	2 (4.9)	2
Severe	1 (2.4)[b]	1
Potentially life-threatening	1 (2.4)[a]	1
TEAEs leading to discontinuation	0	0
TEAEs leading to death	0	0

[a]Participant had a brain neoplasm, which was unrelated to RBL.
[b]Participant had a flare of preexisting ulcerative colitis during the study; assessed as unrelated to RBL.

SECONDARY ENDPOINTS

EFFECTIVENESS

95.1% (39 participants) experienced treatment success (no CDI recurrence through 8 weeks after RBL administration by colonoscopy)

- The remaining two participants (4.9%) had an indeterminate outcome (i.e., neither the protocol-specified definition for treatment success nor treatment failure was met)
- No participants experienced CDI recurrence through 8 weeks after RBL administration delivered by colonoscopy, thus, no data were available for time to CDI recurrence

PHYSICIAN EXPERIENCE AND PERCEPTION[a]

Physicians' experiences were predominantly favorable, with 90.2% indicating they had a 'positive' (n=23) or 'very positive' (n=14) overall experience when administering RBL via colonoscopy[b]

- Among the 39 participants who completed their 8-week follow-up visits, all (100%) were evaluated by the physicians as either 'very much improved' (n=26; 66.7%) or 'much improved' (n=13; 33.3%) according to CGI-I scores
- Overall, physicians reported that administering RBL via colonoscopy was straightforward and described the process as quick, easy, and well-tolerated by participants

SUMMARY

The authors concluded:

- These exploratory findings suggest that RBL administered via colonoscopy is a practical, safe, and effective option for preventing CDI recurrence in adults
- The safety findings were consistent with previous RBL trials despite the difference in administration method
- Results support the potential clinical utility of RBL delivered by colonoscopy to prevent CDI recurrence

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This publication was supported by Ferring Pharmaceuticals Inc.

CGI-I, Clinical Global Impression – Improvement.

[a] All investigators completed a physician experience questionnaire through a qualitative telephone interview.

[b] Ease of passage through the colonoscope and time required for material preparation were cited as contributing to these 'positive' or 'very positive' experiences by 36.6% (n=15) and 29.3% (n=12) of physicians.

[c] Served as investigators in the CDI-SCOPE study, which was funded by Ferring Pharmaceuticals Inc.

[d] Full-time employees at Ferring Pharmaceuticals Inc.

Please scan this QR code to view the full publication.

Please scan this QR code for full Prescribing Information for the FDA-approved use of REBYOTA® (fecal microbiota, live-jslm) via rectal administration.

REFERENCE

Khanna S, Yoho D, Van Handel D, et al. Safety and effectiveness of fecal microbiota, live-jslm (REBYOTA®) administered by colonoscopy for prevention of recurrent *Clostridioides difficile* infection: 8-week results from CDI-SCOPE, a single-arm, phase IIIb trial. *Therap Adv Gastroenterol*. 2025:18:17562848251339697. doi:10.1177/17562848251339697.

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