Efficacy and Safety of RBX2660 for the Prevention of Recurrent *Clostridium difficile* Infection: Results of the PUNCH CD 2 Trial

Erik R. Dubberke, MD, MSPH, a Christine Lee, MD, b Robert Orenstein, DO, c and Sahil Khanna, MBBS, MS d Gill Hecht, MD, e Joseph Fraiz, MD f

aDepartment of Medicine, Washington University School of Medicine, St. Louis, MO; bHamiltont Regional Laboratory Medicine Program, Department of Pathology and Laboratory Medicine, McMaster University, Hamilton, ON, Canada; cDivision of Infectious Diseases, Mayo Clinic in Arizona, Phoenix, AZ; dDivision of Gastroenterology and Hepatology Mayo Clinic, Rochester, MN; eDivision of Gastroenterology and Nutritional, Loyola University Medical Center, Chicago, IL; fInfectious Disease of Indiana, Carmel, IN

Background

- Experience indicates microbiota-based therapies are highly efficacious at preventing *Clostridium difficile* CDI recurrences.
- There is need for high-quality data on efficacy and safety.
- The PUNCH CD 2 trial was a randomized, placebo-controlled, double-blind study to assess the safety and efficacy of RBX2660, a microbiota-based drug targeted at recurrent CDI.

Methods

- Patients with recent CDI recurrence were randomized to: 2 doses of RBX2660 (Group A); 2 doses of placebo (Group B); or 1 dose of RBX2660 and 1 dose of placebo (Group C) via enema with doses 7 days apart.
- Control of CDI symptoms with antibiotics was required prior to enrollment.
- Antibiotics were discontinued 24-48 hours prior to the first enema.
- Failures could receive up to 2 doses of open-label active treatment, 7 days apart, Figure 1.

Figure 1. PUNCH CD 2 Trial Design

Results

- A total of 127 patients at 21 sites in the U.S. and Canada were enrolled between December 10, 2014 through November 13, 2015 were included in the intent-to-treat analysis:
  - Group A (2 doses of RBX2660): n=41
  - Group B (2 doses of placebo): n=44
  - Group C (1 dose of RBX2660 and 1 dose of placebo): n=42
- The median age was: 63.5; range: 18-92 years; 62% female; median prior CDI episodes: 4; range: 1-6, Table 1.

Efficacy

- **Blinded:**
  - Group C (1 dose) was superior to Group B/placebo (66.7%, 28/42 vs. 45.5%, 19/42, P=0.046).
  - The combined success in Groups A and C (1 or 2 doses) was superior to Group B/placebo: 63.9%, 53/85 vs. 50.6%, 43/85.

- **Open-label:**
  - Of patients in Group A and C who went on to receive open-label treatment, 79% succeeded (31/39).
  - 42 patients who failed placebo (experienced recurrences) went on to receive open-label treatment with RBX2660. Of these patients, 87.5% (21/24) were successful when treated with RBX2660.

- **Overall:**
  - For all patients who were randomized to receive at least 1 active treatment (Groups A and C), the overall success (blind and open-label was 89% (n=789) compared with a 45% (25/56) placebo response, P<0.001, Figure 2.

Safety

- There were 580 adverse events (AEs) reported in 54 patients and 45 serious AEs in 26 patients with a mean follow-up of 8.3 months, Table 2.
- AEs were primarily gastrointestinal (93.7%, 529/580).
- There were no unanticipated AEs and there was no significant difference in proportion of AEs or serious AEs among the treatment groups.

Definition of Success (4 All Criteria Required)

- Presence of diarrhea, with or without other CDI symptoms, at 4-6 weeks after last treatment
- A positive stool test for *Clostridium difficile*
- Based for re-treatment for CDI
- No other cause for diarrhea identified

Objectives

- Assess dosing strategy for RBX2660
- Efficacy of 1 vs. 2 doses of RBX2660
- Long-term safety of RBX2660

Major Inclusion Criteria

- Age: 10 years or older at the date of enrollment
- A positive stool test for *Clostridium difficile* within 60 days prior to enrollment
- At least two recurrences of CDI after a primary episode
- At least two episodes of severe CDI resulting in hospitalization

Major Exclusion Criteria

- History of inflammatory bowel disease (ulcerative colitis, Crohn’s disease or microscopic colitis); irritable bowel syndrome; chronic diarrheal disease; colostomy
- Evidence of active colitis
- Known exposure to antibiotics within 6 months after study enrollment
- Compromised immune system
- White blood cell count <1,000 cells/µL

RBX2660

- Microbiota-based drug manufactured from low human-derived microbes using standardized processes and controls
- Each unit of RBX2660 is identified by a unique batch number and is traceable to a specific donor and recipient

Definition of Success

- The absence of *Clostridium difficile* diarrhea - without the need for retreatment with a *Clostridium difficile* anti-infective therapy or fecal transplant through 8 weeks after administration of the second dose of the assigned treatment in the blinded phase

Definition of Failure (All 4 Criteria Required)

- Presence of diarrhea, with or without other CDI symptoms, at 4-6 weeks after last treatment
- A positive stool test for *Clostridium difficile*
- Based for re-treatment for CDI
- No other cause for diarrhea identified

Conclusions

- RBX2660 administered via enema is a safe and effective and effective treatment for recurrent CDI.
- Overall efficacy of RBX2660 was 89.2% in a randomized, double-blind, placebo-controlled trial in patients with recent recurrence.
- AEs were primarily gastrointestinal; there were no unanticipated AEs.
- RBX2660 provided a durable cure.

The results were consistent with those achieved in the open-label PUNCH CD trial.

References


The PUNCH CD 2 trial was sponsored by Rebiotix Inc., Novo Nordisk, Inc.