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,[d] Gail Hecht, MD,[e] Joseph Fraiz, MD[f]

[a] Department of Medicine, Washington University School of Medicine, St. Louis, MO; [b]Hamilton Regional Laboratory Medicine Program, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada; [c]Division of Infectious Diseases, Mayo Clinic in Arizona, Phoenix, AZ; [d]Division of Gastroenterology and Hepatology Mayo Clinic, Rochester, MN; [e] Division of Gastroenterology and Nutrition, Loyola University Medical Center, Chicago, IL; [f]Infectious Disease of Indiana, Carmel, IN

Background
Restoration of the intestinal microbiota is highly efficacious in preventing recurrent *Clostridium difficile* Infection (CDI). RBX2660 is a microbiota-based drug targeted at recurrent CDI. PUNCH CD 2, a multicenter, randomized, placebo controlled, double-blinded Phase 2b trial was conducted to evaluate the safety and efficacy of RBX2660 including questions about dosing strategy and enema administration.

Methods
Patients were randomized to receive either: 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. The primary end point was treatment success following 2 doses of RBX2660 compared with 2 doses of placebo. Success was defined as the absence of *Clostridium difficile*-associated diarrhea at 56 days following completion of the assigned treatment. Failures could receive up to 2 doses of open-label active treatment, 7 days apart. Secondary end points included overall efficacy and safety. Safety was assessed via a patient diary and clinical assessment.

Results
A total of 150 patients at 21 sites in the US and Canada were enrolled in the study. Of these, 127 patients (Group A: n=41; Group B: n=44; Group C: n=42) were in the intention-to-treat population (mean age 61 years; 62.2% female). Efficacy for Group A was 61% vs. 45.5% for Group B, P= 0.152. Efficacy for Group C was 66.7% compared with Group B (45.5%), P=0.048. Efficacy of Group A and C (63.9%) vs. B (45.5%), P= 0.046.

For patients who developed recurrent CDI after receipt of the study drug, open-label treatment success was: Group A (68.8%, 11/16); Group B (87.5%, 21/24); Group C (71.4%; 10/14) for an overall open label success rate of 77.8%.

The combined efficacy for all patients who received at least 1 active treatment, including those who received open label RBX2660 after initial treatment failure, was 88.8% (n= 95).

Adverse events (AEs) at 56 days were primarily gastrointestinal; there were no unanticipated AEs. There was no significant difference in the proportion of adverse or serious AEs among the treatment groups.

Conclusions

In patients with recurrent CDI, a single dose of RBX2660 was superior to placebo, and showed equivalent efficacy as 2 doses. RBX2660 administered via enema was safe.