Durable Prevention of Recurrent *C. difficile* Infection with RBX2660: Results of the PUNCH CD 2 Trial

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Background:
Antibiotic treatment of *C. difficile* infection (CDI) with standard of care antibiotics is associated with high recurrence rates. Microbiota-based drugs have shown promise in durable prevention of CDI recurrence.[1] We report on the durability of RBX2660 for the prevention of recurrent CDI in in a post-hoc analysis of PUNCH CD 2, a Phase 2b a randomized, double-blinded, placebo-controlled trial.

Methods:
Patients enrolled in the PUNCH CD 2 trial were randomized to receive either: 2 doses of RBX2660 (a microbiota-based drug manufactured from live human-derived microbes); 2 doses of placebo; or 1 dose of RBX2660 and 1 dose of placebo via enema with doses 7 days apart. The placebo consisted of normal saline and cryoprotectant in the same proportions found in RBX2660. Success was measured as the absence of CDI symptoms at 8 weeks post treatment. Failures in any study group were eligible to receive open-label treatment with up to 2 doses of RBX2660. Failure was defined as recurrent *C. difficile*-associated diarrhea; positive CDI stool test; need for retreatment for CDI; no other cause for CDI symptoms. Patients will be followed to 24 months after completing the last treatment.

Results:
A total of 107 patients (median age 63, range: 18-92 years; 59.8% female) at 21 centers in the U.S. and Canada received at least 1 dose of RBX2660 with an overall success rate of 88.8% (95/107). Of these patients, 4.2% (4/95) developed a new episode of CDI confirmed by a positive test > 8 weeks after the last RBX2660 treatment. One episode occurred after the patient was treated with antibiotics for a dog bite; another during a hospital stay for small bowel obstruction; and 2 were of unknown origin.

The long-term CDI-free rate (median follow-up: 8.3 months; range 1.6 to 14.9 months) was 95.8% (91/95), Table 1. The median time to a new CDI episode was 135, range: 61-259 days after treatment with RBX2660.

Discussion:
Recurrent CDI poses on-going treatment challenges with high recurrence rates after standard antibiotic treatment. RBX2660, a microbiota-based drug, was demonstrated as an efficacious treatment for recurrent CDI with long-term durability in both open-label and randomized controlled trials. Long-term follow-up is ongoing.

References
1. Orenstein R, Dubberke E, Hardi R, et al. Safety and Durability of RBX2660 (Microbiota Suspension) for Recurrent *Clostridium difficile* Infection: Results of the PUNCH CD Study. *Clin Infect Dis.* 2016;62:596-602.

Table 1. Durability of RBX2660 Treatment Per Follow-Up Milestone

	Overall	3 Months	6 Months	12 Months
Long-term infection-free rate %, n,N	95.8 91/95	98.9 90/91	95.7 67/70	87.5 14/16