The Microbiota-based Drug RBX2660 is Efficacious and Safe in Patients with Recurrent *Clostridium difficile* Infections: Results from 2 Controlled Clinical Trials

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Background
Recurrent *Clostridium difficile* infections (rCDI) are an urgent public health threat with limited effective treatment options. RBX2660 is a microbiota-based drug being developed to prevent rCDI. Herein we compare results from two Phase 2 controlled trials to evaluate the safety and efficacy of RBX2660.

Materials / Methods
In a double-blinded multi-center Phase 2 clinical trial (PUNCH CD2), patients were randomized to receive either 2 RBX2660, 1 RBX2660 dose + 1 placebo dose, or 2 placebo doses. This trial included an open-label phase in which patients who failed blinded treatment could receive $\leq$2 additional RBX2660 doses. In a subsequent multi-center open-label study (PUNCH SOS), patients received $\leq$2 doses of RBX2660, and their outcomes were compared to patients who only received standard-of-care antibiotic treatment in matched historic antibiotic-treated controls. Both studies enrolled patients with ≥2 prior rCDI or ≥2 prior CDI episodes requiring hospitalization. The primary efficacy endpoint for both studies was absence of CDI at 8 weeks from the last dose or from conclusion of antibiotic treatment for the control arm. Safety was assessed via patient diaries and clinical assessment, or by chart review for the control arm.

Results
369 rCDI patients were evaluated across both trials. In the first trial, the efficacy among patients who received $\geq$1 blinded RBX2660 treatment was 66.7% (n=83) compared to 45.5% for placebo-treated patients (n=42; $p<0.05$). The efficacy among patients who received $\geq$1 RBX2660 in the open-label phase was 77.8% (n=54). In the second multi-center trial, efficacy among patients who received $\geq$1 RBX2660 treatment was 79.4% (n=136), compared to 51.8% in the Control group (n=110; $p<0.001$). Adverse events (AEs) within 8-weeks post-treatment were primarily gastrointestinal with no unanticipated AEs. There were no significant differences in the proportion of AEs or serious AEs among treatment groups within each trial. Furthermore, demographic variables of age, sex, or geographic location did not contribute to patient outcome in either trial.

Conclusion
Collectively, these controlled Phase 2 clinical trials demonstrate safety of RBX2660 in rCDI patients and effectiveness of RBX2660 in preventing rCDI when compared to placebo-treated and historical control groups.

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