

Next Generation Fecal Transplant for Recurrent *C. difficile* Infection with and without Antibiotic Pre-Treatment: Lessons Learned from the PUNCH CD Phase 2 Safety Study

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Background: Fecal transplant (FT) is a promising non-antibiotic treatment option for refractory/recurrent *Clostridium difficile* infection (CDI) and is gaining increasing acceptance. However, the optimal protocol for FT is yet to be determined. We report on enema administration of RBX2660 (microbiota suspension), a next generation fecal transplant, for the treatment of recurrent CDI, with or without antibiotic pre-treatment in the context of the PUNCH CD phase 2 safety study.

Methods: RBX2660 was administered via enema to patients with recurrent CDI within 24-48 hours after completion of a 7-day course of oral vancomycin to bring their CDI under control. No pre-enema bowel prep was required. A second RBX2660 enema treatment was permitted if CDI recurred in < 8 weeks. Antibiotics for CDI were not prescribed prior to the second treatment, and RBX2660 was administered to patients with active CDI. Enema administration was chosen as it carries less risk than sedated procedures.

Results: Thirty-four patients (mean age 66.8 years; range 26.7 to 89.6 years; 67.6% female) were enrolled in the study. Thirty-one patients received at least one RBX2660 treatment and were included in the 60-day interim analysis. Efficacy of the first enema defined as the absence of CDI at 8 weeks was 52% (16/31). Efficacy increased markedly for the second dose when antibiotics were not present to 78.6% (11/14), representing a 51% improvement. Overall efficacy was 87.1% (27/31). Enema administration was simple and well tolerated. There was no difference in the incidence of adverse events after treatment with RBX2660 with and without antibiotic pretreatment, and there were no serious adverse events related to the treatment in either case.

Conclusions: This first prospective multi-center study of a biologic drug containing a suspension of live intestinal microbes for recurrent CDI demonstrated that enema administration with or without antibiotic pre-treatment is safe. Overall efficacy results were comparable with those reported for fecal transplant in the literature.

Subject Category: A5.Treatment of HAIs/antimicrobial resistant infections; C1. Clinical trials; N8 *Clostridium difficile*

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