

Enema Administration of RBX2660 (microbiota suspension) for Recurrent *C. difficile* Infection: Lessons Learned from the PUNCH CD Study

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Purpose: Fecal transplantation is gaining increasing acceptance as an effective method of treating recurrent *Clostridium difficile* infection (CDI). However, there are many unknowns about the therapy including questions about administration. Administration via colonoscopy, nasogastric or nasoduodenal tube, and enema have been reported in the literature. Definitive superiority has not been established for any one method.

We report on lessons learned about enema administration of RBX2660 (microbiota suspension) for the treatment of recurrent CDI in the context of a 60-day interim analysis of the PUNCH CD phase 2 multicenter safety study. RBX2660, a biologic drug consisting of live human-derived microbes, is a next generation version of fecal transplantation.

Methods: RBX2660 was administered via enema to unprepped patients with recurrent CDI who were treated with standardized vancomycin. A second RBX2660 treatment was permitted if CDI reoccurred in <8 weeks. Antibiotics were not required prior to the second treatment. Enema administration was chosen because of simplicity, convenience and safety compared with colonoscopic or nasoenteral administration which are associated with additional risk, especially in the recurrent CDI population (elderly with multiple comorbidities).

Results: A total of 34 patients (mean age 66.8 years; range 26.7 to 89.6 years) received at least one RBX2660 treatment, and 31 were included in the 60-day interim analysis (2 patients dropped out after the first dose and 1 died of respiratory failure). Overall efficacy was 87.1%. The most common position for enema administration was left lateral decubitus (used in 94.1% of patients for the first treatment and in 100% for the second treatment). The knee/chest position was used in the remaining cases. The mean time patients remained in position after RBX2660 administration was 44.5 min. (range 15.0-75 min.) for the first treatment; 47.7 min. (range 15.0-60 min.) for the second treatment. Forceful enema expulsion was reported in 4 patients after the first treatment and in 4 after the second treatment. The mean retention time prior to expulsion was 15.8 min. for the first treatment and 7.8 min. for the second treatment. Six of the 8 patients who expelled the enema were treatment successes. A patient who expelled only a small amount of the enema 20 minutes after treatment and a second patient who expelled a moderate amount 5 minutes after treatment were treatment failures.

Conclusions: Enema administration of RBX2660 in the first multicenter study of a biologic drug containing live human-derived microbes was simple and well tolerated with efficacy results consistent with those reported in the literature for fecal transplantation.