Lack of Association with Patient Demographics and Outcomes in PUNCH CD 2, a Randomized Controlled Trial of RBX2660, a Microbiota-Based Drug for Recurrent *Clostridium difficile* Infection

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Background: Microbiota therapy is gaining acceptance to prevent recurrent *Clostridium difficile* infection (CDI) in multi-recurrent subjects. The PUNCH CD 2 study was a randomized, double-blind placebo-controlled study of RBX2660, a microbiota-based drug, which demonstrated both safety and efficacy over placebo. Recent microbiota-based drug trials have suggested demographic differences on treatment outcome. We investigate four key demographic stratifications (age, gender, geographic location, and type of antibiotic used pre-enrollment) of subjects enrolled PUNCH CD 2 and their associations with patient outcome.

Methods: Patients enrolled in the PUNCH CD 2 were >18 years old, had at least two recurrences of CDI after a primary episode, and had completed at least two rounds of standard-of-care oral antibiotic therapy or had at least two episodes of severe CDI resulting in hospitalization. Patients were randomized to: 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, doses 7 days apart. CDI symptoms were controlled with antibiotics prior to enrolment, but were discontinued 24-48 hours prior to the first dose of RBX2660. Demographic information was collected at time of enrolment, with success and failure designation applied after the study blind was lifted. Logistic regression was used to determine probability of demographic impact on success.

Results: A total of 127 subjects at 21 centers in the United States and Canada were randomized and received treatment in the blinded phase of the study. Demographics, clinical variables and patient outcomes (Table 1) were fit to a logistic regression model and demonstrated that treatment success was dependent only on treatment type received (active versus placebo). Age, gender, geographic site of administration, and type of antibiotic use pre-enrollment were not significant in determining patient outcome.

Conclusion: Patients who received RBX2660 were more likely to have treatment success after controlling for confounders. Patient age, gender, geographic location, and type of antibiotic used pre-enrollment did not have a statistically significant impact on patient outcome regardless of treatment type in this randomized, double-blind placebo-controlled study.