RBX Abstract for ASM Microbe 2017

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Resetting the Microbial Landscape: Donor Microbiome Engraftment in Patients Treated with RBX2660 for Multi-Recurrent *Clostridium difficile* Infection

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Background: Recurrent *Clostridium difficile* infections (rCDI) are associated with decreased taxonomic diversity in patients' intestinal microbiome compared to healthy microbiomes. RBX2660 is a standardized microbiota-based drug manufactured from live human microbes and designed to rehabilitate a patient's intestinal microbiota. This abstract describes whether the RBX2660 defines microbiome for subjects treated in PUNCH CD2—a randomized, double-blind, placebo-controlled study evaluating RBX2660 for the prevention of rCDI.

Methods: Subjects were randomized to receive 2 doses of RBX2660 (Group A), 2 doses of placebo (Group B), or 1 dose of RBX2660 and 1 dose of placebo (Group C) by enema, with doses 7 days apart. Each RBX2660 dose originated from a single donor-traceable lot manufactured from one of 19 possible donors. Voluntary stool samples were collected from all subjects at baseline and at 7, 30, and 60 days after treatment.

Relative taxonomic abundances at the class level were determined using 16s rRNA sequencing of 113 stool samples collected from 42 subjects in Groups A and C, and of 136 product samples from the 19 RBX2660 donor lots utilized in the study. Relative abundance data from subject samples were grouped longitudinally and compared to RBX2660 data using a Bray-Curtis dissimilarity calculation with non-metric multi-dimensional scaling. Additional analyses were performed based on the Dirichlet-Multinomial distribution to compare group mean relative taxonomic abundances, pi, and within group over dispersion, theta.

Results: The 19 RBX2660 donor lots had similar taxonomic distributions, with a group mean that was distinctly different from subjects' baseline microbiomes. After treatment, the group means of subjects' microbiomes progressed to more closely resemble the RBX2660 group mean over time, with the largest shift observed 7 days after treatment. Moreover, the relative abundances of key taxonomic classes became more related to RBX2660 with increasing time post-treatment (Figure 1). However, regardless of donor lot received, the mean subject microbiome did not completely converge to the mean RBX2660 microbiome by day 60 post-treatment.

Conclusion: RBX2660 microbiomes contribute to, but do not fully define, a subject's post-treatment microbiome. Further work is needed to define specific taxa and strains that directly engraft from RBX2660 to patient and to evaluate whether early engraftment correlates with eventual treatment response.

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Figure 1. ML estimates (MLE) of pi for Donor and Patient Microbiomes following RBX2660 Treatment