RBX Abstract for ACG2017

Altering the Microbiome: Patients with a Successful Outcome Following Microbiota-Based RBX2660 Treatment Trend Toward Human Microbiome Project Healthy Subjects' Profile

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Introduction

Recurrent *Clostridium difficile* infections (rCDI) are strongly associated with intestinal dysbiosis. RBX2660 is a standardized microbiota-based drug designed to prevent rCDI by potentially restoring a healthier intestinal microbiome. The effect of RBX2660 on rCDI patient microbiomes was evaluated by comparing pre- and post-treatment samples collected from a Phase 2 open-label study of RBX2660 to a healthy intestinal microbiome defined by the Human Microbiome Project (HMP).

Methods

Patients with ≥2 CDI recurrences following ≥2 courses of standard-of-care antibiotic therapy or ≥2 episodes of severe CDI that required hospitalization were enrolled and received 2 doses of RBX2660 delivered via enema 7 days apart. Success was defined as no CDI recurrence through 56 days after completion of treatment. Stool samples were collected at baseline and at 7, 30, and 60 days after treatment.

16s rRNA sequencing analysis with primers specific for the V4 variable region (Illumina MiSeq platform) was conducted for stool samples from a patient subset. Operational taxonomic units (OTU) data were grouped longitudinally and compared to HMP data using a Bray-Curtis dissimilarity calculation with non-metric multi-dimensional scaling. Group mean microbiomes and relative OTU abundances at the class level were calculated with the Dirichlet-Multinomial distribution and compared among groups using a generalized Wald-type test. Shannon and Simpson(SS) diversity indices were compared among groups using a paired Wilcoxon test. Divergence between group mean microbiomes was estimated and visualized using a Kullback-Leibler divergence (KLD) analysis model (BioRankings, St. Louis, MO).

Results

RBX2660 efficacy was 78.8%. Pretreatment patient microbiomes were less diverse and more divergent from the HMP (healthy) microbiome, with specific taxonomic distributions that were consistent with previous microbiome analyses of rCDI patients. At day 7 after RBX2660 treatment, the SS diversity indices increased compared to baseline. Patient microbiomes diverged from baseline and became more closely related the HMP based on KLD analysis. Similar trends continued to 60 days after RBX2660 treatment. A larger shift from baseline microbiome was seen in responders to RBX2660 compared to non-responders.

Discussion

Results show that RBX2660 treatment shifts patient microbiomes closer to the HMP definition of a healthy microbiome, confirming that RBX2660 can stimulate microbiome rehabilitation.

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