RBX Abstract for IDWEEK 2017

Microbiome Profile is Distinct in Patients with Successful Response to Microbiota-Based Drug RBX2660 Relative to Placebo Responders

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Background
Recurrent *Clostridium difficile* infections (rCDI) are associated with an altered microbiome composition and diversity compared to healthy patients. RBX2660, a standardized microbiota-based drug designed to rehabilitate patients' microbiomes, was superior to placebo for preventing rCDI in a Phase 2B clinical trial (64% vs 46% recurrence free at 56 days). Herein we assessed whether RBX2660 and placebo induced similar or different microbiome changes among patients classified as responders.

Methods
Patients received blinded treatment of 2 doses of RBX2660 (Group A), 2 doses of placebo (Group B), or 1 dose of RBX2660 and 1 dose of placebo (Group C), with doses 7 days apart, and submitted stool samples at baseline, 7, 30, and 60 days after the second treatment. 16s rRNA analysis was performed on samples from 57 patients classified as responders (A, n=21; B, n=15; C, n=21). Microbiome data for all patients at study entry were combined as a treatment-naïve baseline. Groups A and C were pooled as "active" and compared to placebo treatments longitudinally. Microbiome divergence from baseline was determined with Kullback-Leibler (KL) analysis, mean group microbiomes and relative taxonomic abundance at the class level were determined using the Dirichlet-Multinomial distribution and compared with a generalized Wald-type test, and Shannon and Simpson diversity indices were compared with a two-sample Wilcoxon test.

Results
At 7, 30, and 60 days, microbiomes from RBX2660-treated patients had high KL divergence from baseline and significantly different means from baseline ($P<0.001$). Placebo-treated patient microbiomes were less divergent from baseline, with group means significantly different from baseline at 7 and 60 days, but not 30 days. RBX2660 increased the relative abundances of Bacteroidia and decreased Gammaproteobacteria and Bacilli more than placebo. No significant differences in diversity indices were observed among treatment groups.

Conclusion
RBX2660 treatment for rCDI is associated with greater changes in patient microbiomes than placebo treatment, underscoring the potential benefits of microbiome restoration therapy. Longer-term studies are needed to compare the durability of microbiome changes and recurrence-free rates.

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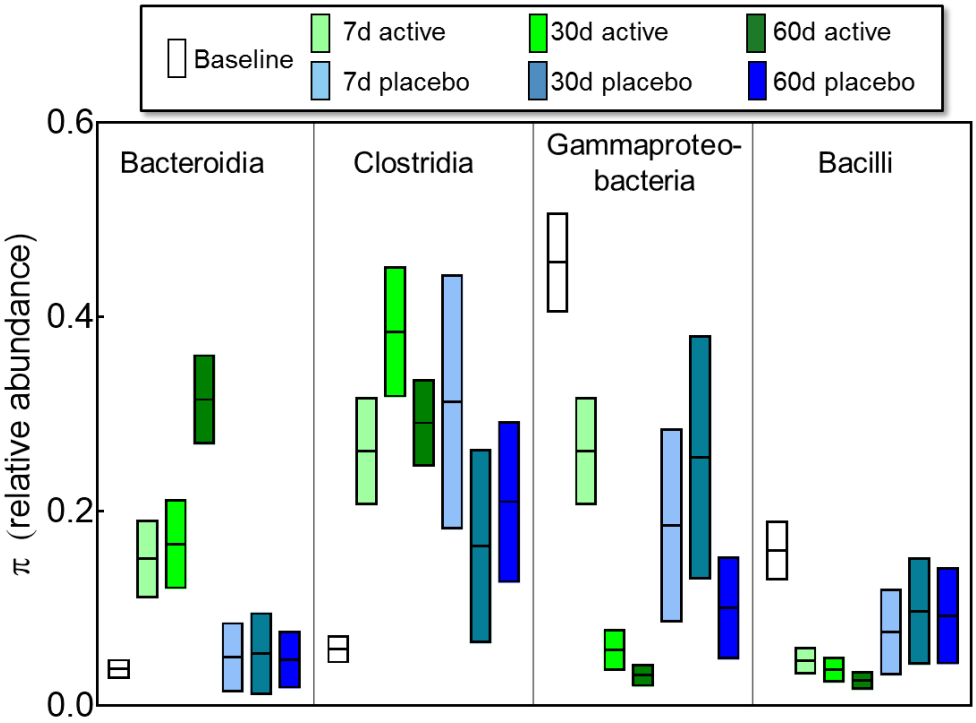
Baseline
7d active
7d placebo
30d active
30d placebo
60d active
60d placebo
Bacteroidia
Clostridia
Gammaproteo-
bacteria
Bacilli
π (relative abundance)
0.6
0.4
0.2
0.0