Response to Microbiota-Based Drug RBX2660 is Associated with Reduction in Antimicrobial Resistance Genes in Patients with Recurrent Clostridioides difficile Infections

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BACKGROUND
• Antibiotic microbial resistance (AMR) is a global health challenge, and is common in recurrent Clostridioides difficile infection (rCDI) population due to high historical exposure to antibiotics.
• The gut microbiota implicated as a reservoir of AMR bacteria.
• Therapeutic approaches that decolonize AMR gut bacteria would be valuable.
• In a previous analysis, RBX2660, an investigational standardized microbiota-restoration therapy in clinical development for preventing rCDI decreased vancomycin-resistant enterococci colonization.

Herein, we assessed the total AMR gene profile before and after treatment in fecal samples from RBX2660 treatment responders in a Phase 2 rCDI trial.

METHODS
• PUNCH Open Label™ (NCT02589847) - prospective, multicenter, open-label Phase 2 study assessing the efficacy and safety of RBX2660 treatment of rCDI: • PATIENT POPULATION: multi-recurrent CDI (≥2 recurrent episodes at enrollment).
• TREATMENT: two doses of RBX2660 administered 7 ± 2 days apart.
• EFFICACY: absence of CDI recurrence at 8 weeks after last study treatment.
• FAILURE: documented recurrence, including positive laboratory diagnosis for C. difficile.
• CONTROL GROUP: historical chart review of patients who only received antibiotic treatment.

Sample set represents 17 trial sites from US and Canada.

All samples were frozen without stabilizers after collection, extracted, and sequenced using a shallow shotgun method.

Sample set includes 66 longitudinally matched samples from 22 treatment-responsive participants, including before treatment (BL) and 7 days and 30 days after treatment. Sample set represents 17 trial sites from US and Canada.

All samples were frozen without stabilizers after collection, extracted, and sequenced using a shallow shotgun method.

Sequencing reads were compared to a proprietary database of gene sequences annotated as related to antimicrobial resistance (CosmosID)

≥40% sequencing coverage of an AMR gene was considered positive identification in each sample.

AMR gene coverage for participant samples were compared to Human Microbiome Project (HMP) data for which comparable sequencing depth was simulated.

RESULTS
• AMR gene decreases were present among broad functional classes.

RBX2660 IS EFFICACIOUS & DURABLE
• 119 of 149 RBX2660-treated participants (80%) were responders at 8 weeks after treatment
• 57 of 110 patients (52%) in the historical control group were recurrence-free 8 weeks after antibiotic treatment

Histological Context RBX2660-treated
9 weeks 8 weeks

• Only 3 of 109 evaluable primary RBX2660 responders reported reinfection at 6 months.
• 97% of RBX2660-treated 8-week responders who were evaluable at 6 months remained recurrence-free.
• Follow up ongoing to 24 months.

RBX2660 SHIFTS MICROBIOME COMPOSITION

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