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**Antimicrobial Resistance Genes Are Reduced Following Administration of Investigational Microbiota-Based Therapeutic RBX7455 to Individuals with Recurrent *Clostrioides difficile* Infection**

Dana Walsh PhD1, Carlos Gonzalez MS2, Bill Shannon PhD MBA2, Ken Blount1

1 Rebiotix Inc, Roseville, MN, USA; 2 BioRankings, St. Louis, MO, USA

**BACKGROUND**Antimicrobial resistance (AMR) is a challenge in individuals at risk for recurrent *Clostrioides difficile* infection (rCDI). Recognizing that AMR bacteria colonize the intestinal microbiota, therapeutic approaches that decolonize the gut of AMR bacteria would be valuable. Herein, we assessed the microbial resistome before and after treatment with RBX7455—a room temperature-stable, orally-administered investigational microbiota-based therapeutic—in a Phase 1 trial for reducing CDI recurrence.

**METHODS**This investigator-sponsored trial enrolled 30 rCDI patients in 3 open-label treatment groups (n=10 per group): 1) Four RBX7455 capsules BID for 4 days, 2) Four RBX7455 capsules BID for 2 days, 3) Two RBX7455 capsules BID for 2 days. RBX7455 administration began 48 hours after finishing CDI antibiotics. Participants were asked to submit stool samples at baseline, 1, 7, 28 and 56 days after treatment. These were extracted and sequenced using a shallow shotgun method. Relative taxonomic abundances at the class level and the presence of AMR genes were determined for 148 participant samples and 11 product samples using 90% K-mer sequence coverage based on the MEGARes database.

**RESULTS**Ninety percent of participants met the primary endpoint of no CDI recurrence through 8 weeks after treatment, and participant microbiome compositions became more similar to RBX7455 after treatment. The total AMR counts per participant decreased from before to after treatment (*p*<.05, mixed effects model), with the pattern of AMRs identified (resistome) becoming more like the RBX7455 resistome (Figure 1). Most notably, AMRs associated with multi-drug, fluoroquinolone, and betalactam resistance decreased from before to after treatment. There was no significant difference among the groups with respect to clinical response or changes in microbiome composition and AMR content.

**CONCLUSION**In a Phase 1 trial of RBX7455 for rCDI, AMR gene content decreased after treatment. This underscores the potential of microbiota-based therapies for decolonizing AMR bacteria from the gut microbiota. Continued clinical evaluation of RBX7455 is underway.

**Figure 1 –** Average total and per-class AMR gene counts in participant samples before and after RBX7455 treatment.

 