

Conclusion. In a trial of RBX2660 for rCDI, participant BA compositions significantly changed from before to after treatment, remained so for at least two years, and correlated with treatment outcome. The resulting predominance of secondary BAs coincided with microbiome compositional changes. Because secondary BA are thought to repress *C. difficile* colonization, these changes may partly explain how RBX2660 reduced CDI recurrence. Continued evaluation of RBX2660 for rCDI is underway.

Disclosures. Romeo Papazyan, PhD, Ferring Pharmaceuticals (Employee) Dana Walsh, PhD, Rebiotix Inc. (Employee) Steve Qi, PhD, Ferring Pharmaceuticals (Employee) Ken Blount, PhD, Rebiotix Inc. (Employee) Karthik Srinivasan, PhD, Ferring Pharmaceuticals (Employee) Bryan Fuchs, PhD, Ferring Pharmaceuticals (Employee)

30. Antimicrobial Resistance Genes Are Reduced Following Administration of Investigational Microbiota-based Therapeutic RBX7455 to Individuals with Recurrent *Clostridioides Difficile* Infection

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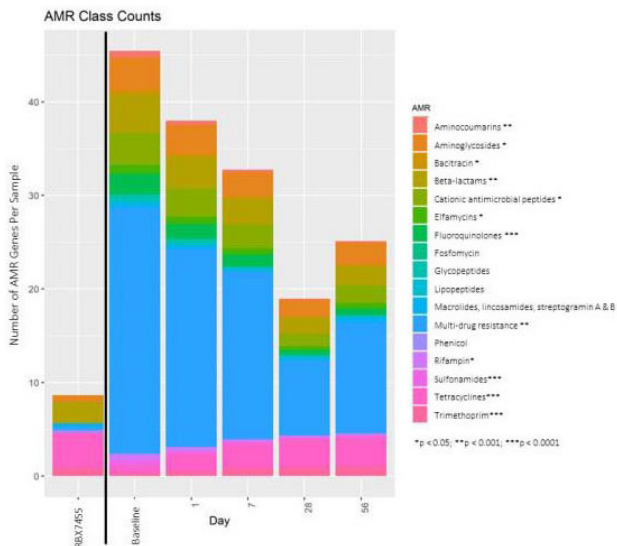
Session: O-6. Antimicrobial insights

Background. Antimicrobial resistance (AMR) is a challenge in individuals at risk for recurrent *Clostridioides 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 beta-lactam 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.

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



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.

Disclosures. Dana Walsh, PhD, Rebiotix Inc. (Employee) Carlos Gonzalez, MS, BioRankings, LLC (Employee) Bill Shannon, PhD MBA, BioRankings, LLC (Employee) Ken Blount, PhD, Rebiotix Inc. (Employee)

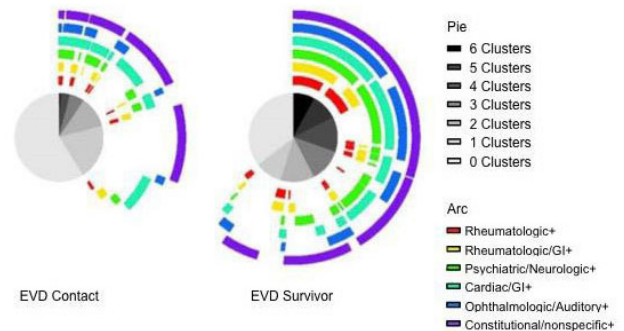
31. Post-ebola Syndrome Presents with Multiple Overlapping Symptom Clusters: Evidence from an Ongoing Cohort Study in Eastern Sierra Leone

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Session: O-7. Around the World - Understanding Infectious Disease and Health Interventions

Background. Since the outbreak of Ebola Virus Disease (EVD) in West Africa from 2013–2016, a large cohort of survivors with persistent health complaints has emerged. This constellation of issues is termed post-Ebola syndrome. Here we characterize the symptoms and physical exam findings of this syndrome in a cohort of survivors from Sierra Leone 2.6 years after resolution of disease.

Ebola survivors present with clusters of symptoms that represent sub phenotypes of post-Ebola syndrome



Methods. Potential survivor participants in Eastern Sierra Leone were identified and recruited through the Sierra Leone Association of Ebola Survivors. Household contacts of survivors were identified by enrolled survivors. Both groups were administered a questionnaire assessing self-reported symptoms. A physical exam was performed by a limited number of trained providers. Symptoms were then compared using hierarchical clustering. Statistical analysis of the correlations between clusters was conducted using conditional logistic regression. Both SPICE and principal component (PCA) analyses were performed to explore the relationships between symptom clusters.

Results. Between March 2016 and January 2019, 375 Ebola survivors and 1040 contacts were enrolled. At enrollment, Ebola survivors of all age groups reported significantly more symptoms than their contacts in all categories. Six symptom clusters were identified representing distinct organ systems. SPICE revealed 2 general phenotypes: with or without rheumatologic symptoms. Clusters including rheumatologic symptoms were correlated with one another ($r = 0.63$) but not with other clusters ($r < 0.35$). Ophthalmologic/auditory symptoms were moderately correlated with the non-rheumatologic clusters ($r > 0.5$). Interestingly, psychologic/neurologic, cardiac/GI and constitutional clusters correlated with one another ($r > 0.6$) $p < 0.0001$ in all cases. The symptom clusters were then mapped onto a PCA. Each symptom cluster separated from the remainder along PC1, particularly the phenotypes with rheumatologic symptoms.

Conclusion. This study presents an in-depth characterization of post-Ebola syndrome in Sierra Leonean survivors. The interrelationship between symptom clusters indicates that post-Ebola syndrome is a heterogeneous disease. The phenotypes identified may have unique mechanisms of pathogenesis, and require distinct therapies.

Disclosures. John Schieffelin, MD, MSPH, Wolters-Kluwer (Independent Contractor)

32. Risk Factors for Vertical Transmission of *t. Cruzi* infection in an Endemic Setting

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Session: O-7. Around the World - Understanding Infectious Disease and Health Interventions

Members of the Chagas Disease Working Group in Peru and Bolivia include: Edith Hinojosa, Clariza Chavez, Jean Karla Velarde, Carla Chavarria, Victoria Serrudo, Roberto Araya, Alcides Buitron, Rita Mendieta, Holger Mayta, Maritza Calderon, Holger Mayta and Yagahira Castro.

Background. Vertical transmission of *Trypanosoma cruzi* infection accounts for a growing proportion of new cases of Chagas disease. Congenital infection is curable if