SATURDAY
AAR-563

Improvement of Microbiome Health Index in Patients with Recurrent *Clostridioides difficile* Infections Following RBX2660 Treatment is Associated with a Reduction in Antimicrobial Resistance Genes

REBIOTIX, INC.
kblount@rebiotix.com

Courtney Jones BS[1], Ken Blount PhD[1], Tonya Ward PhD[2], Elena Deych MS[3], Bill Shannon PhD MBA[3]

[1]Rebiotix Inc., Roseville, MN, USA; [2]CoreBiome, Minneapolis, MN USA; [3]BioRankings LLC, St. Louis, MO, USA

BACKGROUND

- RBX2660, a standardized, stabilized microbiota restoration drug has been shown to prevent recurrent *Clostridiodies difficile* infections (rCDI).
- A preliminary analysis demonstrated decolonization of multidrug-resistant organisms (MDRO) in association with clinical response.
- In parallel, we are developing a Microbiome Health Index (MHI™) to monitor dysbiosis and microbiome restoration.
- Given the public health challenges related with MDROs, we evaluated MHI as a potential sentinel of MDRO colonization among rCDI patients who responded to RBX2660 in a Phase 2 clinical trial.

METHODS

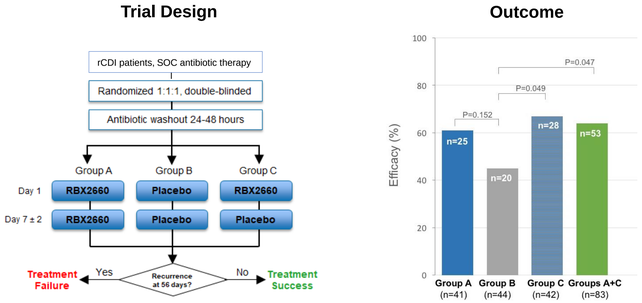
- The PUNCH CD2 Phase 2 trial (NCT02299570) compared RBX2660, a microbiota-based investigational drug for treatment of rCDI, to placebo.
- 127 participants were enrolled, randomized, and treated in three cohorts: Group A: two doses of RBX2660; Group B, two placebo doses; Group C, one dose of RBX2660 and one dose of placebo.
- Samples were collected prior to treatment (BL) and 7, 30 & 60 days after treatment.
- This analysis is based on samples from 55 patients who responded to RBX2660 treatment in Groups A and B (pooled) and dosed RBX2660 product samples.
- Stool samples were sequenced using BoosterShot (CoreBiome, Minneapolis, MN), an ultra-shallow shotgun sequencing method.
- Microbiome Health Index (MHI) values were calculated based on relative abundances at the class level for selected classes.
- Prior receiver operator characteristic analyses defined an MHI cut-point of 8.2 for distinguishing rCDI subjects prior to treatment from the representative microbiome composition of RBX2660.
- Relative abundance of antimicrobial resistance (AMR) genes and enzymes were determined for all samples based on a threshold of ≥90% coverage when compared to the MEGARes database (http://megares.meglab.org)

Microbiome Health Index™ (MHI)

a unidimensional algorithm which captures changes in the relative abundance of taxonomic classes known to have relevance to microbiome health and colonization resistance

RBX2660 EFFICACY IN A PHASE 2 CONTROLLED TRIAL

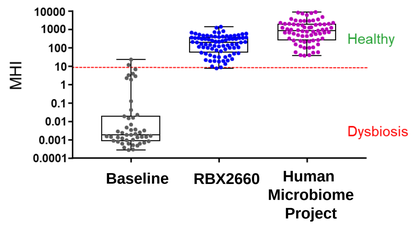
PUNCH CD2: RBX2660 was effective at preventing recurrent CDI



Two doses of RBX2660 was no more effective than one dose (Group A vs Group C). Treatment with one or two doses of RBX 2660 (Pooled A&C) was more effective than placebo.

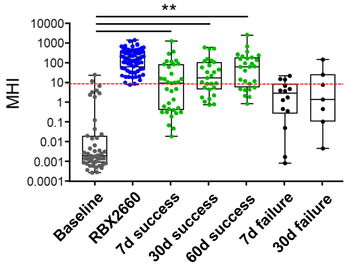
MICROBIOME HEALTH INDEX (MHI) ANALYSIS

MHI can distinguish between baseline "unhealthy" and "healthier" microbiota



Receiver Operating Characteristic (ROC) analysis of baseline (BL) vs RBX2660 product yielded an optimal threshold of MHI=8.2 for distinguishing dysbiosis from healthier as defined by the RBX2660 product profile and the Human Microbiome Project.

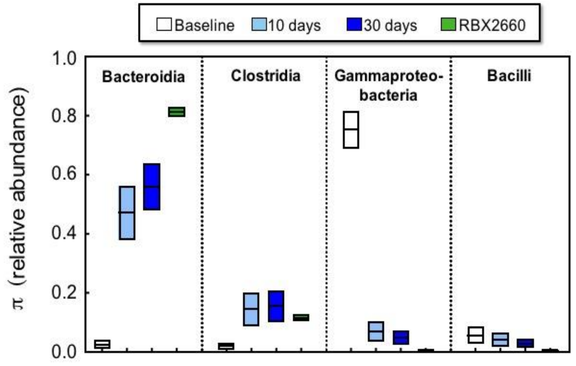
MHI differs among successful and failed response to RBX2660



*** p <0.001 by Sign pairwise test compared to baseline*

MICROBIOME COMPOSITION SHIFTS POST-RBX2660

Taxa levels from PUNCH CD2 participants with successful response to RBX2660 approach product profile levels over time

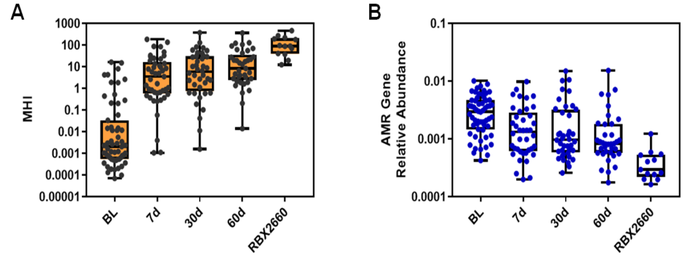


Taxa comparisons were made at the class level using Dirichlet multinomial parameter (pi) representing the group's mean relative taxa abundance, at each time point.

RELATIONSHIP BETWEEN MHI AND ANTIMICROBIAL RESISTANCE GENES

Increase in MHI parallels decrease in AMR gene abundance in RBX2660 responders

RBX2660 response in rCDI patients is associated with restoration of a healthier taxonomic composition as represented by an MHI increase that approached RBX2660 product MHI (A). In parallel, AMR gene relative abundance decreased following RBX2660 treatment to levels similar to the RBX2660 product (B). A similar decrease was observed in the relative abundance of AMR enzymes after treatment.



CONCLUSIONS

- MHI can effectively distinguish patients with dysbiosis from healthier patients, as defined by the RBX2660 product profile and the Human Microbiome Project.
- MHI inversely correlates with AMR gene abundance in a cohort of rCDI patients who had successful response to RBX2660.
- These results suggest MHI as a potential sentinel of MDRO colonization, and this role will be evaluated in future cohorts outside of the rCDI patient population.