Abstract #57150

Title: Impact of RBX2660 on the Intestinal Microbiota of Patients with Recurrent *Clostridium difficile* Infection Enrolled in the Randomized Placebo-Controlled PUNCH CD 2 Trial

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Submitter's E-mail Address: hguthertz@aol.com

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Applying for:

I do not want to apply for any awards or grants. *No changes will be allowed after the May 17 deadline.*

Courtney Jones, BS[1], Bill Shannon, PhD, MBA[2] and Sharina Carter, BS[2], (1)Rebiotix Inc., Roseville, MN, (2)BioRankings LLC, St. Louis, MO

Background: Perturbation of the intestinal microbiota, primarily by antibiotics, sets the stage for *Clostridium difficile* infection (CDI). Restoration of a variable intestinal microbiota protects against recurrence. The impact of RBX2660 on the gut microbiota of patients with recurrent CDI was evaluated in PUNCH CD 2, a multicenter, randomized, double-blinded, placebo-controlled, dose-ranging, phase 2b study.

Methods: Patients with recurrent CDI were randomized to receive either: two doses of RBX2660 (Group A); two doses of placebo (Group B); or one dose of RBX2660 and one dose of placebo (Group C). RBX2660 is a microbiota-based drug manufactured from live human-derived microbes and targeted at the prevention of recurrent CDI. All therapies were administered via enema with doses 7 days apart. Success was defined as the absence of *Clostridium difficile*-associated diarrhea (CDAD) at 56 days.

Longitudinal 16s rRNA analysis was performed on stool samples (n=120) from a total of 75 patients (Group A: n=23; Group B: n=22; Group C: n= 22) at baseline, 7 days and 30 days after the second dose of the blinded therapy sequence using the Illumina MiSeq platform. The variable region V4 was targeted to identify the operational taxonomic units (OTUs) in each sample.

Results: OTU analysis demonstrated higher diversity between baseline and follow-up time points for all patients who responded successfully to their assigned treatment. This included Group B-two doses of placebo – in which 12 patients did not experience recurrent CDI symptoms prior to 56 days. Specifically, successful Group A patients had an increase in *Akkermansia* and *Bacteroides* from baseline; successful Group B and C patients had a decreased abundance of *Enterobacter*. Of the three groups of patients, those in Group A (two doses of active treatment) showed the greatest increase in bacterial diversity (number of OTUs) and abundance of taxa between baseline and all follow-up points.

Conclusion: In this randomized controlled study of RBX2660 for recurrent CDI, 16s rRNA analysis found that patients who succeeded with their assigned therapy had a more diverse intestinal microbiota at 7 and 30 days compared with baseline.

First Author

Presenting Author
Courtney Jones, BS
Program Manager:
Rebiotix Inc.
2660 Patton Road
Roseville, MN 55113
Phone Number: 651-705-8774
Alternate Phone: 651-705-8774
Email: cjones@rebiotix.com

Biographical Sketch: Courtney Jones is the program manager at Rebiotix. She developed and manages the donor program for RBX2660(microbiota suspension), a next-generation fecal microbiota suspension drug. Jones has also taken a lead role in educatiing and informing the public about current research on the human microbiome via several social media channels.

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Second Author

Bill Shannon, PhD, MBA
Founder and Managing Partner, Analytics:
BioRankings LLC
4041 Forest Park Ave.
St. Louis, MO 63108
Phone Number: (314) 633-1821
Alternate Phone: 314-704-8725
Email: bill@biorankings.com

Biographical Sketch: Bill has over 25 years of experience developing analytical methodology for complex and big data in biomedical R&D. He started BioRankings™ in 2014 to work on a broader range of industry projects, and has grown the company to support a staff of dedicated and knowledgeable employees. In his capacity as a Professor of Biostatistics in Medicine at Washington University School of Medicine in St. Louis, Bill focuses on statistical methods grants in emerging areas of medicine, and works with researchers when there are no known statistical methods for analyzing their study data.

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Third Author

Sharina Carter, BS
BioRankings LLC
4041 Forest Park Ave,
St. Louis, MO 63108
Phone Number: (314) 633-1821
Alternate Phone: (314) 633-1821
Email: Sharina@biorankings.com -- Will not be published

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