RBX2660 is Safe, Superior to Antibiotic-Treated Controls for Preventing Recurrent Clostridioides difficile, and May Rehabilitate Patient Microbiomes: Open Label Trial Results

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Background

- Effective treatment options for recurrent C. difficile infection (CDI) are limited
- High recurrence rates are associated with the current standard of care
- RBX2660, a standardized microbiota-based drug, was efficacious for preventing CDI in a double-blinded Phase 2 clinical trial (PUNCH CD 2)

Methods

- Prospective, multi-center, open-label Phase 2 study (NCT02158667)
- Inclusion criteria: >18 years old with documentation of either 2 recurrences after a primary episode and has completed at least two rounds of standard of care oral antibiotic therapy, or at least 2 episodes of severe CDI resulting in hospitalization; a positive stool test for the presence of C. difficile within 60 days prior to enrollment
- Exclusion criteria: History of innate bowel inflammatory bowel disease (ulcerative colitis, Crohn’s disease or microscopic colitis), irritative bowel syndrome, chronic diarrhea; recent history of antibiotic use; known exposure to antibiotics within 6 months after study enrollment; compromised immune system (white blood cell count <1000 cells/µL)

Microbiome Analysis

- Patients in the RBX2660 treatment arm only submitted stool samples at baseline, following RBX2660 treatment, 30 days after treatment, and 30 days after outcomes were assessed
- Stool samples were collected using BooterGooth (Cologen, Minneapolis, MN); an ultra-violet light sequencing that generates taxonomic profiles with species-level resolution
- The variable region V3 was targeted to identify the operational taxonomic units (OTUs) in each sample
- Relative abundance data from successful patients were grouped longitudinally and compared using multidimensional correspondence analysis with non-metric multi-dimensional scaling

Controlled Trials

- Subjects who matched key inclusion/exclusion criteria of the clinical study but who were only treated with standard of care antibiotics for powered efficacy analysis of RBX2660
- Conducted by Loyola University, Mayo Clinic Arizona, Mayo Clinic Rochester, and Mid-Atlantic Permanent Research Institute

Results

- Reported results from a subsite open-label trial that evaluated
  - Safety and efficacy of RBX2660 for preventing CDI relative to matched historical controls
  - Microbiome altering-activity of RBX2660

Hypothesis

- RBX2660’s efficacy in preventing rCDI (78.8%) was higher than CDI-free rates of-care oral antibiotic therapy, or at least 2 episodes of severe CDI resulting in hospitalization; a positive stool test for the presence of C. difficile within 60 days prior to enrollment

- Safety was assessed via a patient diary: in clinic at 1, 4, and 8 weeks and via telephone at 2, 3, between 5-7 weeks, and at 3, 6, 12 and 24 months

- Microbiota analysis suggests that RBX2660 may
  - Alter the RBX2660 microbiome profile than at baseline. Notably, the relative difference to a specific donor and recipient

Conclusion

- This open label Phase 2 study demonstrates RBX2660’s efficacy in preventing CDI compared to an antibiotic-treated historical control group
- The RBX2660 safety profile is consistent with results from previous clinical trials
- Microbiota analysis suggests that RBX2660 may rehabilitate patient microbiota

References

- Orenstein RD et al. Poster# 1863, 2019 AAGL Annual Meeting

TABLE 1: BASELINE AND DEMOGRAPHICS

<table>
<thead>
<tr>
<th>Variable</th>
<th>RBX2660 (N=136)</th>
<th>Historical Control (N=110)</th>
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<tbody>
<tr>
<td>Key Safety Events</td>
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<td></td>
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<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Male</td>
<td>65 ± (19-105)</td>
<td>67 ± (21-170)</td>
</tr>
<tr>
<td>Female</td>
<td>22.6</td>
<td>36.9</td>
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<tr>
<td>Source of Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI Recurrence (%)</td>
<td>50/119 (41.6%)</td>
<td>67/66 (20.5%)</td>
</tr>
<tr>
<td>Healthcare Contagion (%)</td>
<td>23/32 (72%)</td>
<td>32/35 (73%)</td>
</tr>
<tr>
<td>Community Contagion (%)</td>
<td>19 (2.6)</td>
<td>33 (5.6)</td>
</tr>
<tr>
<td>Mean of peak C. difficile days</td>
<td>65.8 [19-103]</td>
<td>67.8 [21-97]</td>
</tr>
</tbody>
</table>

Key Safety Events

- 132 RBX2660 and 110 historical control subjects were enrolled in 20 centers and 44 centers, respectively (USA CA-19)
- RBX2660’s efficacy in preventing CDI (78.8%) was higher than CDI-free rates in the historical control group (51.8%)
- A total of 482 adverse events (AEs) were reported by 99 RBX2660 subjects (75.3%) compared to 91 AEs among 69 historical controls (62.7%)
- Following RBX2660 treatment, RBX2660 treated subjects’ microbiomes were significantly altered compared to baseline and more closely resembled the RBX2660 microbiome profile than at baseline; histopathologically, the relative proportions of Bacteroides and Clostridium increased after treatment, while the relative proportions of Gamma proteobacteria decreased (Figure 2)

Microscopy from patients with recurrent CDI shift towards product profile microorganisms from previous baseline (Fig. 3)

Microscopy from patients with successful response to RBX2660 approach microorganisms profiles over time (Fig. 4)

Table 3: SAFETY EVENTS BY SOURCE

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<th>Source of Infection</th>
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DISCLAIMER

This analysis was funded by Rebiotix Inc., Roseville, MN.