Efficacy was defined as the absence of CDI at 8 weeks after the last treatment.

Donations were not pooled. Donations were made on site at Rebiotix Inc., Roseville, MN. Sourcing and Traceability

Raw material human stool

Supplied in 50g/150 mL dose; ready-to-use enema format

• Fecal microbiota transplantation (FMT) is becoming an increasingly accepted therapy for recurrent Clostridium difficile infection (CDI).

• Overall resolution rates in the range of 100% have been reported in the literature though multiple doses may be necessary to achieve this cure rate.

• There are still many unknowns about the therapy including questions about donor vs. patient factors in therapy success.

• Conventional procedure has been to use a second donor in case of treatment failure.

• The relative importance of the donor was assessed in the context of a Phase 2 study of a next-generation FMT drug.

Results

• A total of 34 patients with recurrent CDI enrolled at 11 sites in the U.S. received 1 or 2 doses of RBX2660 (microbiota suspension) via enema between August 2013 and January 2014 as part of the PUNCH CD study.

• Per protocol, a second dose was permitted if symptoms recurred ≤ 8 weeks after the first dose.

• Patients who required 2 doses could receive RBX2660 manufactured from the same or different donors. The same pair of donors could also be used in a different order.

• Efficacy was defined as the absence of CDI at 8 weeks after the last treatment.

• A mathematical model was used to determine whether the specific donor affected the results.

RBX2660 (microbiota suspension)

• Designed to mimic FMT
• Raw material human stool
• Formulated to have a long shelf life
• Supplied in 50g/150 mL dose; ready-to-use enema format
• Contains a minimum guaranteed quantity of live microbes
• Manufactured using standardized, quality-controlled processes

Sourcing and Traceability

• Four donors were used to prepare the RBX2660 used in the study.

• Donations were made on site at Rebiotix Inc., Roseville, MN.

• Donations were not pooled.

• The same batch was used in 1–4 patients.

• Donors were randomized to patients for both the first and second doses.

• The product was manufactured in donor-specific batches that could be tracked to individual patients and outcomes.

Background

• Fecal microbiota transplantation (FMT) is becoming an increasingly accepted treatment for recurrent Clostridium difficile infection (CDI).

• Conventional procedure has been to use a second donor in case of treatment failure.

• The relative importance of the donor was assessed in the context of a Phase 2 study of a next-generation FMT drug.

Mathematical Model

• A mixed model was used to predict treatment success taking into account donor and dose number.

• Repeated measures data was included to account for patients who received 2 doses of RBX2660. In this analysis, a patient was classified as either a success or failure for both doses.

• Donor 1 was used as the reference donor for comparative purposes as no evidence was seen that the other donors had a different success rate.

• P < .05 indicates statistical significance; all analyses were done using the R statistical package.

Case Study: Same Donor; Same Batch; Different Results

Patient: 89-year-old white female with history of recurrent diarrhea.

Medical History:

• CDI diagnosed during an emergency room visit, positive for toxin A.

• Clostridium difficile hydroxide 500 mg, not tolerated; completed two 10-day courses of metronidazole 500 mg tid; two 14-day courses of vancomycin. 125 mg qid; and 1 course of fidaxomycin, 200 mg bid, without resolution of symptoms.

• FMT was recommended; the patient was enrolled in the PUNCH CD study.

RBX2660 Administration:

• Sept. 16, 2013: first dose; well-tolerated; stool normalized.

• Sept. 30, 2013: CDI symptoms return.

• Oct. 3, 2013: second dose without antibiotic pre-treatment; well-tolerated.

Follow-up:

• No CDI symptoms through 6-month follow-up.

LOGISTIC REGRESSION MODELING FOR ALL PATIENTS AND ALL DOSES

<table>
<thead>
<tr>
<th>Intercept</th>
<th>Est.</th>
<th>Std. Error</th>
<th>z Value</th>
<th>p-Value</th>
<th>P(1–z)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1.724</td>
<td>0.771</td>
<td>0.753</td>
<td>0.585</td>
<td>0.569</td>
<td>0.441</td>
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<tr>
<td>As factor – Dose 2</td>
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<td>0.934</td>
<td>-0.123</td>
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<td>As factor – Donor 4</td>
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<tr>
<td>As factor – Donor 5</td>
<td>16.221</td>
<td>2267.846</td>
<td>0.007</td>
<td>0.999</td>
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</tbody>
</table>

- Donor 5 contributed a comparatively small number of doses and was not significant compared to donor 1. There was a large standard deviation resulting from the small sample size.

- All P values in the logistical model were > .05, indicating no donor effect.

LOGISTIC REGRESSION MODELING FOR PATIENTS RECEIVING 2 DOSSES OF RBX2660

<table>
<thead>
<tr>
<th>Intercept</th>
<th>Est.</th>
<th>Std. Error</th>
<th>z Value</th>
<th>p-Value</th>
<th>P(1–z)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.554</td>
<td>0.711</td>
<td>2.186</td>
<td>0.029</td>
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<tr>
<td>As factor – Dose 2</td>
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<td>2.709</td>
<td>0.007</td>
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<tr>
<td>As factor – Donor 3</td>
<td>0.559</td>
<td>0.872</td>
<td>0.641</td>
<td>0.522</td>
<td></td>
</tr>
</tbody>
</table>

- Donor 3 contributed a comparatively small number of doses and was not significant compared to donor 1. There was a large standard deviation resulting from the small sample size.

- All P values in the logistical model were > .05, indicating no donor effect.

Conclusions

• Based on an analysis of small numbers, it appears that the specific donor does not affect the outcomes achieved with administration of RBX2260 for recurrent CDI.

• The results suggest that outcomes are patient-specific and it is not necessary to switch donors in order to achieve a cure if the first dose fails.

• Additional research with a larger patient cohort along with in-depth comparative analysis of donor and patient microbiota is needed to provide more details on patient-specific factors impacting success or failure with this therapy.

REFERENCES


