THE IMPACT OF INVESTIGATIONAL PURIFIED MICROBIOME THERAPEUTIC SER-109 ON HEALTH-RELATED QUALITY OF LIFE (HRQoL) OF PATIENTS WITH RECURRENT CLOSTRIDIOIDES DIFFICILE INFECTION (rCDI) in ECOSPOR-III, A PLACEBO-CONTROLLED CLINICAL TRIAL

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Disclosures

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Background

- *Clostridioides difficile* infection (CDI) and especially recurrent CDI has been shown to have a significant impact on patient’s physical, psychological, social, professional and financial status.\(^1\)

- SER-109, an investigational oral microbiome therapeutic of purified bacterial spores, was designed to reduce CDI recurrence.
  - ECOSPOR-III, a Phase 3, double-blind, randomized trial, demonstrated the superiority of SER-109 compared to placebo in the reduction of rates of CDI recurrence at Week 8, the primary endpoint.\(^2\) The observed safety profile of SER-109 was comparable to placebo.\(^3\)
  - However, whether SER-109 also improves health-related quality of life (HRQoL) is unknown.

- HRQoL was an exploratory endpoint in the ECOSPOR-III trial.
- Herein, we present a preliminary analysis of these data.

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ECOSPOR-III
Phase 3 Double-blind, Placebo-Controlled Trial of SER-109 for Multiply rCDI

281 adult subjects with ≥2 CDI recurrences were screened
182 toxin+ adult subjects with symptom resolution on antibiotics at enrollment
10 oz magnesium citrate administered prior to randomization to minimize residual antibiotic
Subjects stratified by age and antibiotic received

4 Capsules once daily for 3 Days

Primary endpoint
Recurrence at 8 weeks

Safety through 24 weeks

Recurrences evaluated through 24 weeks

Adult Study Participants ≥18 Years

- Toxin testing required at study entry and at suspected recurrence to ensure enrollment of patients with active disease and accurate assessment of endpoint
- All subjects had acute infection
- No chronic suppressive antibiotics allowed

ClinicalTrials.gov Identifier: NCT03183128
SER-109 was Superior to Placebo in Reducing CDI Recurrence at Week 8

- SER-109 met the primary endpoint of superiority compared to placebo
- The number needed to treat (NNT) for SER-109 is 3.6

Relative risk reduction of 68%

<table>
<thead>
<tr>
<th></th>
<th>Percent Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>SER-109</td>
<td>12.4% (n=89)</td>
</tr>
<tr>
<td>Placebo</td>
<td>39.8% (n=93)</td>
</tr>
</tbody>
</table>

Relative risk (RR) = 0.32 [95% CI 0.18-0.58]; p<0.001 for RR<1.0; p<0.001 for RR<0.833

Objective

- To evaluate the impact of SER-109 versus placebo on HRQoL using a disease-specific measure, Cdiff32.4

EQ-5D-5L and CDiff32 HRQoL Measures

EQ-5D-5L is a general measure used across a wide population of respondents
- Measures 5 health domains
- Used for Baseline Evaluation

CDiff32 is a disease-specific measure which includes content applicable to CDI patients
- Measures 3 health domains
- Primary Outcome Measure
EQ-5D-5L and CDiff32 HRQoL Measures

EQ-5D-5L Anxiety/Depression Questions

- I am not anxious or depressed
- I am slightly anxious or depressed
- I am moderately anxious or depressed
- I am severely anxious or depressed
- I am extremely anxious or depressed

CDiff32 Mental Questions

Anxiety – Current

- I feel that my health is more delicate than other people’s
- Despite my C Diff infection, I can live a normal life
- I feel that I am not in control of my C diff infection

Anxiety – Future

- Are you afraid that the next time you’ll need antibiotics, your C diff infection will appear again?
- Have you been worried about not knowing when the next diarrhea would arise?

*Abstracted questions are sample questions for illustrative purposes*
HRQoL Exploratory Endpoint: By Treatment Group and Clinical Outcome

- Changes from baseline were assessed between SER-109 and placebo and by clinical outcome (recurrence vs. nonrecurrence) in the ITT population and within each treatment arm.
- The between treatment group comparison analysis controlled for age, gender, prior antibiotics, and number of prior CDI episodes.
## Baseline Demographics (ITT Population)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SER-109 (N = 89)</th>
<th>Placebo (N = 93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs), mean (SD)</td>
<td>65.6 (16.5)</td>
<td>65.5 (16.7)</td>
</tr>
<tr>
<td>&lt; 65 years, n (%)</td>
<td>41 (46.1)</td>
<td>38 (40.9)</td>
</tr>
<tr>
<td>≥ 65 years, n (%)</td>
<td>48 (53.9)</td>
<td>55 (59.1)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female*</td>
<td>60 (67.4)</td>
<td>49 (52.7)</td>
</tr>
<tr>
<td>Prior antibiotic, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>64 (71.9)</td>
<td>69 (74.2)</td>
</tr>
<tr>
<td># prior CDI episodes, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>49 (55.1)</td>
<td>61 (65.6)</td>
</tr>
<tr>
<td>≥3</td>
<td>39 (43.8)</td>
<td>32 (34.4)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

N = Population size; n = Number of Subjects.

*More females were in the SER-109 than the placebo arm (p=0.0427)
At Baseline, ECOSPOR-III Patients’ General Health Status is Between Good and Fair Compared to the EQ-5D-5L VAS Norm

- We analyzed 159 HRQoL surveys in this preliminary analysis.
- EQ-5D-5L VAS Norm is defined by the health of the general population and allows for benchmarking of HRQoL status of patients in ECOSPOR-III vs. the general healthy population\(^5\).
- As expected, no differences were observed between groups at follow-up due to the lack of sensitivity of a general HRQoL measure.

HRQoL Measured at Baseline With CDiff32 Was Comparable in Patients Treated with SER-109 or Placebo

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Physical</th>
<th>Mental</th>
<th>Social/Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>SER-109 (n=75)</td>
<td>53.3</td>
<td>66.6</td>
<td>38.2</td>
<td>59.7</td>
</tr>
<tr>
<td>Placebo (n=81)</td>
<td>52.5</td>
<td>66.1</td>
<td>37.8</td>
<td>56.9</td>
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</tbody>
</table>
Regardless of Treatment Group, All Patients Achieved Significant Improvement from Baseline on All CDiff32 Domains by Week 8 With a Greater Magnitude of Change Observed in the SER-109 Group.

Week 8

<table>
<thead>
<tr>
<th>CDiff32 Mean Change from Baseline</th>
<th>SER-109 (n=75)</th>
<th>Placebo (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>17.7</td>
<td>11.3</td>
</tr>
<tr>
<td>Physical</td>
<td>14.2</td>
<td>9.1</td>
</tr>
<tr>
<td>Mental</td>
<td><strong>22.1</strong></td>
<td><strong>14.5</strong></td>
</tr>
<tr>
<td>Social/Relationship</td>
<td><strong>14.3</strong></td>
<td><em>8.33</em></td>
</tr>
</tbody>
</table>

*p<0.05  **p<0.001
Regardless of Treatment Group, Non-Recurrent Patients Had Significant Improvements in All CDiff32 Domains Compared with Recurrent Patients

![Graphs showing improvement in CDiff32 domains over time for recurrent and non-recurrent patients.](chart)

* *p<0.05      **p<0.001              between group comparison
HRQoL in SER-109 and Placebo Patients By Clinical Outcome at Week 8

Placebo Week 8

SER-109 Week 8

Caution due to small number of patients with recurrence

\*p<0.05 \**p<0.001   □ between group comparison
Conclusions

- Significant disease-specific HRQoL improvements were associated with CDI nonrecurrence, which highlights the negative impact of rCDI.
- SER-109 was associated with improved overall and mental health scores compared to baseline regardless of clinical outcome as measured by CDiff32.
- In light of emerging data on the potential impact of the gut microbiome on neurologic diseases, future studies should evaluate whether SER-109 may provide mood and anxiety enhancing properties through modulation of the gut-brain axis.
References


Acknowledgements

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