Investigational Microbiome Therapeutic SER-109 Reduces Recurrence of Clostridioides difficile Infection (rCDI) Compared to Placebo, Regardless of Risk Factors For Recurrence

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Background

- Clostridioides difficile infection (CDI) is a two-hit process characterized by disruption of the microbiome and exposure to C. difficile toxins. The leading risk factor for CDI is exposure to broad spectrum antibiotics, which cause collateral damage to beneficial microbes that normally reside in the GI tract.
- Although C. difficile targets antibiotics rapidly to both producing bacteria, they do not eradicate the metabolically inactive C. difficile spores that germinate in a disrupted microbiome. Thus, a sustained response is not obtained in a substantial proportion of patients who continue to experience recurrent CDI.
- SER-109, a novel investigational oral microbiome therapeutic of purified bacterial spores was developed to reduce CDI recurrence.
- In ECOSPOR II, a Phase 3, double-blind, randomized trial, SER-109 was superior to placebo in reducing CDI recurrence at Week 8, the primary endpoint; SER-109 achieved a 68% relative risk reduction in recurrence rates compared to those treated with placebo (12.4% vs 28.0%, respectively; relative risk [RR] 0.32 [95% CI, 0.18-0.56]; P=0.001 for RR in WHU, 0.10-0.50 for RR in IRU). The observed safety profile of SER-109 was comparable to placebo.
- Several demographic and clinical characteristics, including age, sex, proton pump inhibitor use, and presence of comorbid conditions are considered risk factors for recurrent CDI (CDI). We examined the efficacy of an investigational purified oral microbiome therapeutic, SER-109, versus placebo in an exploratory analysis of subgroups of patients with risk factors for recurrence who enrolled in ECOSPOR II, a double-blind, placebo-controlled trial.

Methods

- Patients with CDI (≥ 1 episode in 12 months) were treated with SER-109 or placebo (four capsules daily for three days) following standard treatment of CDI.
- The primary efficacy objective was to demonstrate superiority of SER-109 versus placebo in reducing CDI recurrence up to 8 weeks after treatment. Safety was evaluated up to 26 weeks after dosing.
- In this exploratory analysis, we assessed the role of CDI recurrence among SER-109 treated subjects compared to placebo subgroup defined by CDI baseline characteristics (proton pump inhibitor use, presence of CDI recurrence, prior FMT history).
- We also analyzed the role of CDI recurrence among SER-109 treated subjects by age (< 65 and ≥65) and gender, which were pre-specified.

Relative Risk of Recurrence at Week 8 for Selected Baseline Characteristics

<table>
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<tr>
<th>Factor</th>
<th>Analysis Model</th>
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<tbody>
<tr>
<td>Age &lt; 65 years old</td>
<td>RR 0.37 (0.17-0.87)</td>
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<tr>
<td>Age ≥ 65 years old</td>
<td>RR 0.45 (0.26-0.79)</td>
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<tr>
<td>Gender Male</td>
<td>RR 0.91 (0.46-1.82)</td>
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<tr>
<td>Gender Female</td>
<td>RR 1.05 (0.51-2.13)</td>
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<tr>
<td>Positive Antibiotic Exposure</td>
<td>RR 0.11 (0.03-0.46)</td>
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<td>RR 0.11 (0.03-0.46)</td>
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<tr>
<td>No Antibiotic Use for CDI</td>
<td>RR 0.67 (0.36-1.25)</td>
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<tr>
<td>No Antibiotic Use for CDI</td>
<td>RR 0.67 (0.36-1.25)</td>
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<tr>
<td>Use Antibiotic Use for CDI</td>
<td>RR 0.11 (0.03-0.46)</td>
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Conclusions

- In ECOSPOR II, SER-109, an investigational live microbiome therapeutic, significantly reduced the risk of recurrence compared to placebo.
- By enriching for specific risk factors, SER-109 met the primary endpoint of reducing CDI while mitigating risk of transmitting infectious agents.
- Regardless of baseline risk factors, SER-109 reduced recurrence of CDI compared to placebo.
- Most subsets in ECOSPOR III had co-morbidities consistent with the broad inclusion criteria in this Phase 3 trial.
- Despite a high proportion of patients with co-morbidities in ECOSPOR III, SER-109 significantly reduced the risk of recurrence compared to placebo.
- SER-109 may represent a potential paradigm shift in the clinical management of patients with recurrent CDI.

An open label study for patients with ≥ 1 episode of CDI is currently enrolling (ClinicalTrials.gov Identifier: NCT03183128).

References


Acknowledgement

The authors thank Dr. David K. Davidson for his assistance in data analysis and preparation of the draft manuscript. The authors are grateful to the patients and investigators who participated in the ECOSPOR II trial.