Conference Poster # 634

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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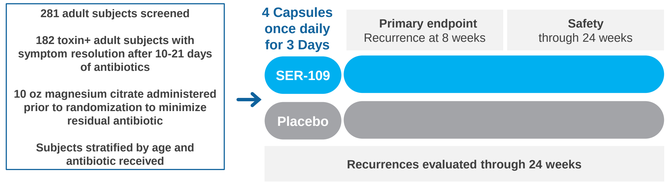
Background

- *Clostridioides difficile* infection (CDI) is a two-hit process characterized by disruption of the microbiome and exposure to *C. difficile* spores. 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.[1]
- Although *C. difficile* targeted antibiotics rapidly kill vegetative toxin-producing bacteria, they do not eradicate the metabolically-inactive C. difficile spores that germinate in a disrupted microbiome. Thus, a sustained response is not attained in a substantial proportion of patients who continue to experience recurrent CDI[2].
- SER-109, a novel investigational oral microbiome therapeutic of purified bacterial spores was developed to reduce CDI recurrence.
- In ECOSPOR-III, a Phase 3, double-blind, randomized trial, SER-109 was superior to placebo in reducing CDI recurrence at Week 8, the primary endpoint.[3] SER-109 achieved a 68% relative risk reduction in recurrence rates compared to those treated with placebo (12.4% vs 39.8%, respectively; 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]). The observed safety profile of SER -109 was comparable to placebo.[4]
- Several demographic and clinical characteristics, including age, sex, proton-pump inhibitor use, and presence of comorbid conditions are considered risk factors for recurrent CDI (rCDI). 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 III, a double-blind, placebo-controlled trial.

ECOSPOR-III

Ph3 Double-blind, Placebo-Controlled Trial of SER-109 for Multiply Recurrent CDI



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

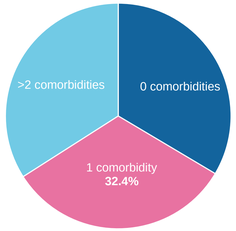
ClinicalTrials.gov Identifier: NCT03183128

Methods

- Patients with rCDI (≥3 episodes 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 rCDI up to 8 weeks after treatment. Safety was evaluated up to 24 weeks after dosing.
- In this exploratory analysis, we assessed the rate of CDI recurrence among SER-109 treated subjects compared to placebo in subgroups defined by rCDI baseline risk factors: proton-pump inhibitor use, number of CDI recurrences, prior FMT history, presence of comorbid conditions and exposure to non-CDI antibiotics after dosing.
- We also analyzed the rate of CDI recurrence among SER-109 treated subjects by age (≥ 65 and <65) and gender, which were pre-specified.

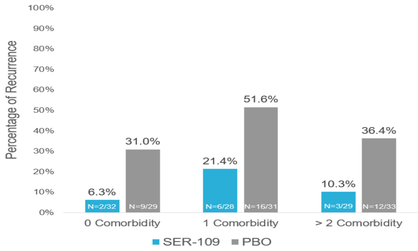
Percentage of Co-Morbid Conditions at Baseline

Figure 1: Percentage of Co-Morbid Conditions at Baseline



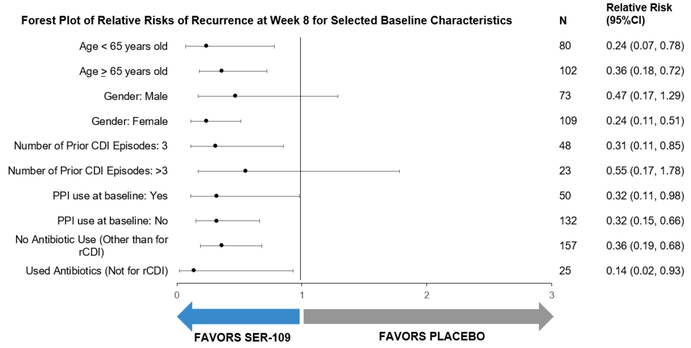
Co-morbidities, including diabetes, renal disease, malignancy, cardiac disease, COPD/asthma, colitis and host immunosuppression were observed in most patients (66.4%)

CDI Recurrence Rates by Number of Pre-Existing Medical Conditions

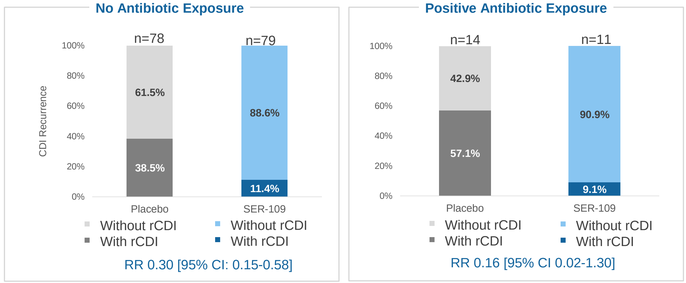


SER-109 was consistently observed to show greater benefit than placebo in reducing CDI recurrence in all subgroups regardless of the presence or absence of the rCDI risk factor.

Relative Risk of Recurrence at Week 8 for Selected Baseline Characteristics



Use of Non-CDI Antibiotics Were Not Associated With Increased CDI Recurrence in SER-109 Patients



Conclusions

- In ECOSPOR III, SER-109, an investigational live microbiome therapeutic, significantly reduced the risk of recurrence compared to placebo.
- By enriching for Firmicute spores, SER-109 met the primary endpoint of reducing CDI while mitigating risk of transmitting infectious agents.
- Regardless of risk factor status, SER-109 reduced recurrence of CDI compared to placebo.
- Most subjects 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: NCT03183141).

References

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