SHEA 2021
Poster 140

EFFICACY AND SAFETY OF INVESTIGATIONAL MICROBE DRUG SER-109 FOR TREATMENT OF RECURRENT *CLOSTRIDIOIDES DIFFICILE* INFECTION (RCDI)

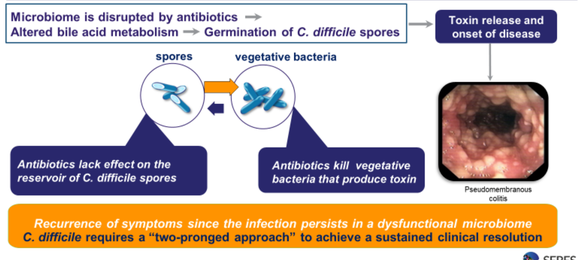
McGovern BH, Sims M, Lashner B, Korman L, Kraft CS, Wang EE, Brady K, Ford CB, O'Brien EJ, Lombardo M-J, Wortman JR, Litcofsky KD, Li D, Mahoney J, McChalicher CW, Winkler JA, Garant S, McMullen E, Aunins JG, Henn MR, Trucksis M and LL von Moltke

SERES THERAPEUTICS™

BACKGROUND

- Since the discovery of *C. difficile* in 1978 as the causative agent of "antibiotic-associated colitis", clinical response rates remain suboptimal, and few drugs have been approved.
- 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 gastrointestinal microbiome.
- Antibiotics targeted against *C. difficile* bacteria are necessary, but insufficient, to achieve a durable clinical response because they have no effect on *C. difficile* spores that germinate within a disrupted microbiome.

C. difficile targeted antibiotics are necessary but insufficient for treatment due to the two-phase life cycle of _C. difficile_



McGovern Clin Infect Dis 2020

- ECOSPOR-III, a Phase 3 double-blind placebo-controlled trial, evaluated SER-109, an oral investigational microbiome therapeutic composed of live purified Firmicutes spores for treatment of patients with recurrent CDI.

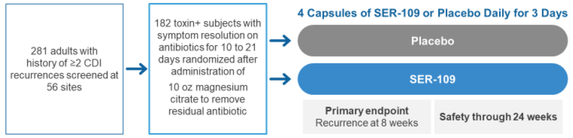
METHODS

- Adults ≥18 years with rCDI (≥3 episodes in 12 months) were screened at 75 US/CAN sites.
- CDI was defined as ≥3 unformed stools/day for ≥48 hours with a (+) C. difficile assay.
- After completion of 10-21 days of vancomycin or fidaxomicin, adults with symptom resolution were randomized 1:1 to SER-109 (4 capsules x 3 days) or matching placebo and stratified by age (≥ or <65 years) and antibiotic received.
- Primary efficacy endpoint was rCDI (recurrent toxin+ diarrhea requiring treatment) up to 8 weeks after initiation of treatment; secondary endpoints included efficacy at 12 weeks after dosing. The safety of SER-109 was evaluated as compared to placebo through 8 weeks after dosing.
- Study patients were stratified by age and by antibiotic received prior to treatment.

RESULTS

Study Design and Study Participants

ECOSPOR-III
Double-blind, placebo-controlled Ph3 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

Demographics
ITT population

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

N = Population size; n = Number of Subjects.

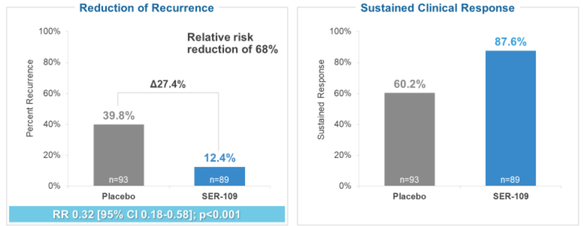
*More females were in the SER-109 than the placebo arm p-value 0.0427

Age, antibiotic use, and number of prior episodes were similar across treatment arms

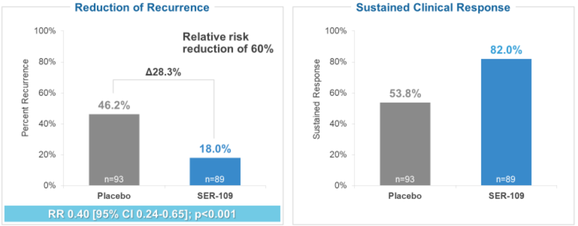
73% of patients overall were treated with vancomycin prior to randomization

60% had history of 2 recurrences before entering with third acute episode; 40% with ≥3 recurrences

SER-109 was superior to placebo in reducing CDI recurrence at week 8



SER-109 was superior to placebo in reducing CDI recurrence at week 12



Safety

Summary of Subjects with Treatment Emergent Adverse Events up to Week 8

	SER-109 (N=90) n (%)	Placebo (N=92) n (%)
Any TEAE	84 (93.3)	84 (91.3)
Subjects with Serious TEAEs Leading to Study Withdrawal	0	0
Treatment Related/Possibly Related TEAEs	46 (51.1)	48 (52.2)
Treatment Emergent AESIs	1 (1.1)	1 (1.1)
Serious TEAEs	7 (7.8)	15 (16.3)
TEAEs leading to Death	2	0
Serious TEAEs or Deaths Related or Possibly Related to Drug	0	0

3 deaths occurred on the SER-109 arm, all reported as unrelated; two patients died within the 8-week period shown above and one patient withdrew from the study and died after week 23.

Conclusions

CDI is a two-hit process that requires a two-pronged treatment approach to prevent rCDI
- Antibiotics to kill the toxin-producing bacteria and
- Microbiome recovery to inhibit spore germination and vegetative growth

SER-109 was highly efficacious in reducing recurrence validating our spore-based therapeutic approach
- The favorable safety profile was comparable to placebo
- SER-109 achieved high efficacy while mitigating risk of transmitting infectious agents

SER-109, an investigational, first-in-class, oral microbiome therapeutic is a promising partner in a new treatment paradigm for patients with recurrent CDI
- An open label trial for first and multiply recurrent patients has been initiated
- Requirements to file SER-109 for product approval are under discussion with the Food and Drug Administration (FDA)