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.

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 × 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.