SER-109, an Oral Microbiome Therapy for Recurrent *Clostridioides difficile* Infection

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**Clinical Problem**
Antibiotics for *Clostridioides difficile* infection can induce microbiome disruption that enables germination of *C. difficile* spores, which can then lead to recurrent infections. A treatment approach that can prevent recurrent infection is needed.

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**Clinical Trial**
Design: A phase 3, double-blind, placebo-controlled trial assessed the efficacy of SER-109 — an investigational oral microbiome therapeutic made up of live purified Firmicutes bacterial spores that could limit *C. difficile* spore germination — in patients with three or more *C. difficile* infections in the previous year.  
Intervention: 182 adults who had symptom resolution after antibiotic treatment for *C. difficile* infection and were at high risk for recurrence were assigned to receive either SER-109 or placebo, given as four capsules once daily over 3 days. The primary end point was recurrence of *C. difficile* infection within 8 weeks.

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**Results**
Efficacy: At 8 weeks, SER-109 was superior to placebo in lowering rates of *C. difficile* recurrence. The benefit was seen in patients 65 years of age or older and in those younger than 65 years of age, as well as in those initially treated with vancomycin or fidaxomicin.  
Safety: The percentages of patients with adverse events were similar in the two groups; most symptoms were gastrointestinal and mild to moderate in nature.  
Limitations:  
- Minority groups were underrepresented.  
- Stool specimens were not obtained before antibiotic treatment, so the full effect of SER-109 on the pre-antibiotic microbiome is unknown.

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**Conclusions**
In patients with recurrent *C. difficile* infection, a two-pronged treatment approach of standard-of-care antibiotics followed by a microbiome-replacement therapy can reduce the risk of recurrence.