IDSE Infectious Disease SPECIAL EDITION

Bacterial Infections

JUNE 25, 2025

ASM Microbe 2025

Competitor to Vancomycin for *C. difficile* May Be Coming Soon

By Marcus A. Banks

The narrow-spectrum antibiotic CRS3123, being developed by Crestone Inc., better preserved gut microbiome diversity than vancomycin in a phase 2 clinical trial of people with *Clostridioides difficile*, according to data presented at the ASM Microbe 2025 meeting, in Los Angeles.

This could potentially lower the risk for *C. difficile* infection (CDI) recurrence. The gut microbiome benefits of CRS3123 were true for both alpha and beta diversity, meaning a greater abundance of microbial diversity at single locations (alpha) and throughout the gut (beta).

The trial compared fecal samples from people with CDI who took CRS3123 with those of patients with the condition who took vancomycin.

"There is significant dysbiosis in patients who are taking vancomycin compared with the patients who are taking CRS3123," said trial investigator **Oren Gordon**, MD, a pediatric oncology fellow at Children's Hospital Colorado, in Aurora, at the meeting.

The biotech company Crestone, in Boulder, Colo., sponsored the randomized, double-blind trial. There were 43 total trial participants, who were at least 18 years of age and balanced by gender, race and ethnicity. Everyone had experienced one or two episodes of CDI. Participants were 58 years of age on average, and 33 of the 43 were women.

Fourteen trial participants took 200 mg of CRS3123 twice daily for 10 days; another 15 participants took 400 mg of CRS3123 twice daily for 10 days; and 14 participants took 125 mg of vancomycin four times daily for 10 days.

Clinically, "CRS3123 seems to be comparable to vancomycin, if not a little bit better," Dr. Gordon said. Both antibiotics significantly reduced levels of the genus *Clostridioides*, which includes the species *C. difficile*, as measured by 16S rRNA sequencing of fecal samples up to 70 days after the trial began. The time to resolve diarrhea symptoms was also similar between groups.

But there was a lower probability of CDI recurrence in people who took CRS3123 compared with those who took vancomycin. That could be because CRS3123 induced a healthier gut.

"CRS3123 better preserves gut microbiome diversity in comparison to vancomycin," Dr. Gordon said, for alpha and beta diversity alike. These included a relative abundance of *Bacteroides* and *Bifidobacterium.*

Dysbiosis could make someone more susceptible to disease recurrence given people with CDI tend to have low levels of alpha diversity and commensal bacteria (*Front Cell Infect Microbiol* 2023;13:1130701).

"The higher the level of alpha diversity, the more diverse and healthier the gut microbiome is in general," Dr. Gordon said.

The infectious disease community has taken note of these findings.

"It is now abundantly clear that curbing *C. difficile* while preserving healthy intestinal flora is what we want in a CDI therapeutic. The outcome of this phase 2 study further reinforces that goal," said **Mark Wilcox**, MD, a professor at Leeds Teaching Hospitals and University of Leeds and the lead on CDI for UK Health Security Agency, when the results were announced. (https://www.businesswire.com/news/home/20240904819996/en/Crestone-Announces-Positive-Data-From-Phase-2-Clinical-Trial-of-CRS3123-for-C.-Difficile-Infections-CDI). Dr. Wilcox is also an advisory board member for *Infectious Disease Special Edition*.

Multiple manuscripts about the study are in development, Dr. Gordon said, about the clinical impact of CRS3123 and its effect on the gut microbiome.