Fidaxomicin is superior to vancomycin in treating recurrences of gastrointestinal *Clostridium difficile* infection, according to a blinded randomized trial presented here at the 50th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC).

"Over 20 years, vancomycin has been the best drug for efficacy [in the treatment of *C difficile* infection. The problem is that the recurrence rate in sick people, like those we included in the study, is about 30%. Now we know we can prevent recurrences after vancomycin with fidaxomicin. Fidaxomicin was also superior as first-line treatment in phase 3 studies. In my view, this is a dramatic change," said Oliver A. Cornely, MD, from the University Hospital of Cologne in Germany.

Fidaxomicin is a first-in-class oral macrocyclic antibiotic developed by Optimer Pharmaceuticals. The drug has a narrow spectrum of activity against normal gut flora, with potent bactericidal activity against *C difficile.* It attacks the pathogenic bacteria while sparing normal protective gastrointestinal flora. In contrast, vancomycin, which is approved for this indication, and metronidazole, which is often used as treatment, suppress the growth of normal endogenous flora.

The study presented at ICAAC focused on a prespecified nested population of 178 patients with a first recurrence within 90 days of a previous episode. Patients were then randomized to receive either fidaxomicin or vancomycin. These 178 patients came from 2 randomized phase 3 trials of 1164 patients with acute *C difficile* infection. In both phase 3 trials, fidaxomicin was noninferior to oral vancomycin in preventing symptom recurrence within 30 days of completing 10 days of therapy.

Recurrence was defined as 3 or more unformed bowel movements in the 24 hours prior to randomization and the presence of *C difficile* toxin A or B in the stool within 48 hours of randomization; this definition was used in the original phase 3 trials and in the nested trial.

For 10 days, patients received oral fidaxomicin 200 mg twice daily or oral vancomycin 125 mg 4 times daily. More than 90% of both groups responded to initial therapy in the phase 3 trials.

In the nested trial, 55% were female, 53% were inpatients, and the mean age was 63 years. Among 122 evaluable patients, fidaxomicin was significantly superior to vancomycin for the primary end point of a second recurrence within 28 days (19.7% vs 35.5%; *P* = .045). Fidaxomicin was also significantly superior to vancomycin in preventing a second recurrence in up to 14 days (7.6% vs 27.4%; *P* = .003).

"Recurrences occurred later with fidaxomicin ð on about day 17 compared with day 8 ð for patients on vancomycin," Dr. Cornely said.

Older age is a known risk factor for recurrent *C difficile*, he continued. In the nested study, patients 75 years and older were 2.7 times more likely to experience a recurrence than those between 18 and 54 years of age. No difference in recurrence rate was seen between patients in the 2 age groups.

Dr. Cornely believes that an explanation for the superiority of fidaxomicin in these studies is that the healthy flora protected against the re-emergence of *C difficile* in patients who received the newer drug, whereas persistent spores of the bacteria remained in the gut of patients who received vancomycin.

"The subgroup analysis of initial studies suggests that fidaxomicin may be a very important tool for preventing recurrence after initial infection, but large prospective trials are needed to address that issue properly," said David M. Aronoff, MD, comoderator of the session in which Dr. Cornely presented the study results. Dr. Aronoff is assistant professor of infectious diseases at the University of Michigan in Ann Arbor.

Dr. Aronoff noted that fidaxomicin might be a good drug for first-line therapy as well. "It may be as effective as vancomycin in treating initial infection, as well as in preventing recurrence."

He said that further study is needed to determine the putative connection between the differential effects of vancomycin and fidaxomicin on the bacterial environment of the gut and whether those differential effects are causally related to the clinical effects of these drugs.

*Dr. Cornely reports serving as a consultant to Optimer Pharmaceuticals, and having ties with other pharmaceutical companies, but none that make anti**ï** C difficile drugs. Dr. Aronoff has disclosed no relevant financial relationships.*

50th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC): Abstract L1-1305. Presented September 13, 2010.