Once-Daily Dosing on Tap for Traveler's Diarrhea

BY DOUG BRUNK

SAN FRANCISCO — Prulifloxacin, a new fluoroquinolone, was superior to placebo in reducing the duration of diarrhea in adult travelers, results from a phase III, randomized, double-blind trial showed.

"This drug is very similar to ciprofloxacin, but we think it has certain advantages, such as its once-a-day dosing," Brian Walsh, D.V.M., said in an interview during a poster session at the annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy. "It's also very safe. We think this is as good as ciprofloxacin in that respect."

Manufactured by Optimer Pharmaceuticals, San Diego, prulifloxacin (Pruli) is currently available in Japan and Italy but not in the United States. The drug's active metabolite, ulifloxacin, has potent activity against gram-negative bacilli, said Dr. Walsh, who is a consultant for the company.

In a trial sponsored by Optimer Pharmaceuticals, he and his associates randomized 268 adults with traveler's diarrhea in India, Guatemala, and Mexico to receive 600 mg prulifloxacin once daily or placebo for 3 days. Study participants recorded stool activity to the test-of-cure visit, which occurred 24-72 hours after the last dose. The primary end point was time to last unformed stool.

The 268 patients comprised the intent-to-treat population. Of these, 200 were eligible for modified intent-to-treat analysis and 173 patients were microbiologically evaluable.

The patients' mean age was 32 years, and 55% were female and 92% were white.

Dr. Walsh and his associates reported that prulifloxacin was superior to placebo for the intent-to-treat, modified intent-to-treat, and microbiologically evaluable patients using a Kaplan-Meier long-rank test for the time to last unformed stool. Among patients treated with prulifloxacin, the median time to last unformed stool was 33 hours in the intent-to-treat group, 33 hours in the modified intent-to-treat group, and 32 hours in the microbiologically evaluable group.

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"Because more than half of the subjects given placebo were clinical failures or did not achieve wellness by the end-of-therapy [test of cure] visit, a median time to last unformed stool could not be estimated for the placebo group," the researchers noted in their poster.

In the modified intent-to-treat population, traveler's diarrhea–associated enteropathogens including enteroaggregative *Escherichia coli*, *Salmonella*, *Campylobacter*, and *Shigella* species were eradicated in 67% of the patients given prulifloxacin and in 27% of the 103 patients given placebo. In the microbiologically evaluable population, these enteropathogens were eradicated in 67% of the 82 patients given prulifloxacin and in 31% of the 91 patients given placebo.

"For this particular suite of pathogens, this is as good as it gets," Dr. Walsh said.

Prulifloxacin and placebo had similar safety profiles. Three patients withdrew from the placebo arm of the study because of serious adverse events: one experienced deep vein thrombosis and pulmonary embolism, one experienced worsening of traveler's diarrhea, and one developed pseudomembranous colitis.

Two additional patients withdrew from the trial because of nonserious adverse events: one from the prulifloxacin group who experienced edema and one from the placebo group who experienced asthenia. All events resolved.

Dr. Walsh said that Optimer intends to submit approval documents for prulifloxacin to the Food and Drug Administration during the first quarter of 2010. ■