New Topical Antibiotic May Thwart Resistance

BY BRUCE JANCIN
Denver Bureau

LISBON — Five days of the novel topical antibiotic retapamulin is as effective in the treatment of uncomplicated skin infections as 10 days of an oral cephalosporin, Dr. Lawrence C. Parish reported at the 12th International Congress on Infectious Diseases.

Patients prefer topical over systemic therapy in this setting by a 3-to-1 margin. When retapamulin ointment becomes available—and GlaxoSmithKline anticipates Food and Drug Administration approval later this year—many physicians will prefer this new option, too, predicted Dr. Parish, a dermatologist at Jefferson Medical College, Philadelphia.

Retapamulin is first in a new class of antibacterials known as pleuromutilins. They possess a novel mechanism of action and an extremely low propensity for development of bacterial resistance.

Retapamulin has excellent activity against gram-positive organisms, including the chief pathogens involved in skin and skin structure infections, such as *Streptococcus pyogenes* and *Staphylococcus aureus,* including the methicillin- and mupirocin-resistant strains. In vitro studies indicate the drug has no target-specific cross resistance to other antibiotic classes, so it's highly effective against bacteria resistant to antibiotics. Retapamulin's oral absorption is poor; it has therefore been developed as a topical agent. Allergy to the product is "almost nonexistent," according to Dr. Parish.

In a study of 546 patients with secondarily infected dermatitis, 5 days of retapamulin ointment were as effective as 10 days of oral cephalexin.

He reported on 546 patients with secondarily infected dermatitis who participated in a phase III, randomized, double-blind, double-dummy clinical trial conducted at 109 centers in North America, Europe, Asia, and Africa.

The patients, among them 124 children and adolescents, were assigned in a ratio of 2:1 to 5 days of retapamulin ointment 1% b.i.d. or 10 days of oral cephalexin at 500 mg b.i.d. in a noninferiority trial involving physicians from multiple specialties. Dr. Parish served as principal investigator.

The primary efficacy end point was clinical response at follow-up on days 17-19. The rates—86% in the retapamulin group and 90% with oral cephalexin—weren't statistically different. Nor were the microbiologic success rates of 87% and 92%, respectively.

Both drugs had 100% microbiologic success in patients with baseline methicillin-resistant *S. aureus,* although there were only seven affected patients, he said at the meeting, which was sponsored by the International Society for Infectious Diseases.

Clinical success rates at the end of therapy were also comparable: 92% in the retapamulin arm on days 7-9, and 94% with oral therapy on days 12-14.

The two therapies were equally well tolerated. No serious adverse events occurred. The most common treatment-related adverse events were treatment-site itching in 1% of the retapamulin group and diarrhea and/or abdominal pain in 1.1% of the cephalexin arm. Participants expressed a 3-to-1 preference for topical over oral therapy for their skin infection.

Dr. Parish said in an interview that the traditional physician preference for oral treatment of bacterial infections and topical therapy for dermatophyte infections isn't based in science.

"I've tried to trace where the prejudice comes from, and I haven't been able to determine it," he said, adding that he believes many physicians, presented with evidence of equal efficacy, would prefer to use a topical medication rather than expose their patients to a systemic antibiotic.

He predicted that the topical pleuromutilin will fill a role in clinical practice similar to that once occupied by mupirocin (Bactroban), which was widely prescribed for the topical therapy of secondarily infected inflammatory skin diseases until resistance became a major problem—a not-surprising development considering the drug has been marketed in the United States for 18 years.

He disclosed no ties to GlaxoSmithKline, but has received payment to conduct clinical research for the company. ■