New Cream May Prevent Cold Sore Recurrence

BY DOUG BRUNK

SAN FRANCISCO — A newly approved cream containing 5% acyclovir and 1% hydrocortisone prevented ulcerated lesions in patients with recurrent herpes simplex labialis, compared with both topical acyclovir and placebo, a large multicenter study showed.

The product, ME-609 (Lipsovir), was approved for marketing in the United States in late July and is indicated for the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten lesion healing time.

"This is the first product to prevent the development of cold sores," Dr. Spotswood L. Spruance said in an interview during a poster session at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy. "Other products have been shown to reduce the duration of the disease, but this has been shown to block the development of ulcers and blisters."

Developed by Medivir of Huddinge, Sweden, ME-609 is not yet available in the United States because Medivir has not yet partnered with a company to distribute and market the product. A company spokeswoman estimated that ME-609 would be available in the United States some time in 2010.

For the study, researchers led by Dr. Christopher M. Hull of the department of dermatology at the University of Utah, Salt Lake City, randomized 1,443 patients aged 18 years and older with at least three episodes of herpes simplex labialis to one of three treatment groups: ME-609 vehicle containing 5% acyclovir and 1% hydrocortisone (n=601), acyclovir alone in ME-609 vehicle (n=610), or placebo (n=232).

The patients were instructed to start treatment at home five times daily for 5 days at the earliest sign or symptom of their next recurrence of herpes simplex labialis, and to keep a diary of symptoms.

The mean age of patients was 44 years, and 28% were male.

Dr. Spruance of the division of infectious diseases at the University of Utah reported that, at the end of treatment, the proportion of patients with nonulcerative recurrences was 42% in the ME-609 group, compared with 35% for acyclovir and 26% for placebo.

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DR. SPRUANCE

Among patients who developed an ulcerative lesion despite treatment, the duration of lesions was reduced by ME-609 to a similar extent as acyclovir alone (a mean of 5.7 days vs. a mean of 5.9 days, respectively); both were significantly shorter than placebo (a mean of 6.5 days), he said at the meeting, which was sponsored by the American Society for Microbiology.

Lesion healing time was reduced by ME-609 to a similar extent as acyclovir alone (a mean of 9.6 days vs. 9.9 days, respectively), with both significantly shorter than placebo (11 days).

The cumulative lesion area was reduced by one-half in the ME-609 group, compared with the placebo group, and the differences in cumulative lesion area between ME-609 and the other two groups were statistically significant.

Frequency of secondary herpes recurrences was 5% in the ME-609 group, 7% in the acyclovir group, and 7% in the placebo group, while the proportion of patients with positive viral cultures was 22%, 24%, and 40%, respectively.

The frequency and nature of adverse events was similar between the groups.

Medivir funded the study. Dr. Spruance disclosed that he is a paid consultant for the company. ■

FDA Approves Gardasil for Boys and Cervarix for Girls

BY LORI BUCKNER FARMER

The Food and Drug Administration has approved the drug Gardasil for boys and men aged 9-26 years, and Cervarix for girls and women aged 10-25 years.

Gardasil was approved for preventing genital warts associated with the human papillomavirus (HPV), according to a statement from the drug's manufacturer, Merck & Co. An FDA press officer confirmed the approval.

HPV vaccine offers protection against four strains of the virus (types 6, 11, 16, and 18) that have been associated with the most disease, including cervical cancer in women (types 16 and 18) and genital warts in both women and men (types 6 and 11), according to the statement.

Gardasil is not recommended for pregnant women or for individuals with hypersensitivity (including severe allergy) to yeast, according to the drug's safety information.

HPV vaccination in males "may be more relevant to dermatologists," said Dr. Stephen K. Tyring, clinical professor of dermatology at the University of Texas Health Science Center in Houston. "We don't get a lot of women asking about the HPV vaccine, but we may see more men." Pediatricians and gynecologists typically counsel and vaccinate girls and women against HPV.

This is "big news in the world of papillomavirus," Dr. Tyring said at the women's and pediatric dermatology seminar sponsored by Skin Disease Education Foundation (SDEF). Dr. Tyring is a consultant, has received grant/research support, and is on the speakers' bureau for Merck and GlaxoSmithKline. SDEF and this news organization are owned by Elsevier.

Cervarix, a recombinant bivalent HPV vaccine was also approved by the FDA for the prevention of cervical cancer and certain precancerous or dysplastic lesions caused by HPV types 16 and 18 in girls and women.

The FDA followed the advice of its Vaccines and Related Biological Products Advisory Committee, which found that data supported the efficacy of the vaccine for preventing HPV 16/18-related cervical cancer, cervical intraepithelial neoplasia (CIN) 2+, and adenocarcinoma in situ (AIS) in girls and women aged 15-25 years.

The vaccine, which will be marketed by GlaxoSmithKline Biologicals as Cervarix, is administered in a three-dose schedule at 0, 1, and 6 months.

The advisory panel also had found that an immunogenicity bridging study from the United Kingdom—which compared immune responses to the vaccine in recipients aged 10-14 years with those of older recipients—supported effectiveness of this same claim in girls aged 10-14 years. There were no efficacy data in the younger age group, but immune responses for HPV 16/18 in the younger girls were similar to those in the older group.

The majority of the panel also voted that the data supported the safety of the vaccine in girls and women aged 10-25 years but recommended that safety issues, which included spontaneous abortions, be studied further after licensure.

In the pivotal study, there were a higher number of spontaneous abortions around the time of vaccination than in the comparison group.

The company has also announced plans to conduct a postmarketing safety study.

There were more musculoskeletal and neuroinflammatory events with potential autoimmune causes—although rare—among almost 30,000 Cervarix recipients, compared with controls. The three most common adverse events associated with the vaccine were headache, injection site pain, and fever. ■

Heidi Splete and Damian McNamara contributed to this report.

Investigational Antibiotic for MRSA Found Effective, Safe

BY ROBERT FINN

SAN FRANCISCO — A short course of therapy with torezolid phosphate cured virtually all patients with *Staphylococcus aureus*–based severe complicated skin and skin structure infections in a randomized, double-blind, phase II study.

A second-generation oxazolidinone related to linezolid, torezolid phosphate is a prodrug that can be given orally once per day, Dr. Philippe Prokocimer said in an interview. Dr. Prokocimer is medical director of Trius Therapeutics, the San Diego–based company that is developing the drug. He was one of the authors of the study, which was presented in a poster at the Interscience Conference on Antimicrobial Agents and Chemotherapy, sponsored by the American Society for Microbiology.

The study involved 192 patients with *S. aureus* infections who were randomized to receive 200 mg, 300 mg, or 400 mg of torezolid phosphate once a day for 5-7 days. All patients had severe complicated skin and skin structure infections (cSSSI, also called acute bacterial skin structure infections), defined as skin infections that were 5 cm or greater in diameter and/or included systemic signs of infection. Patients with uncomplicated disease or with infections requiring gram-negative coverage were excluded, as were immunocompromised patients and those who had used antibiotics for more than 24 hours within 96 hours of the start of the study.

The clinical outcomes were similar in all dosage groups. Of the patients whose lesions were microbiologically evaluable, 96% achieved a clinical cure, including 95.7% of the patients with methicillin-susceptible *S. aureus* infections and 96.9% of the patients with methicillin-resistant *S. aureus* infections.

Five of the patients in the study experienced serious adverse events, but only one of these could have been drug related—a case of acute cholecystitis in an obese 57-year-old woman 2 days after the end of therapy. All other treatment-emergent adverse events were mild or moderate, with nausea the most common (19% of patients). The investigators saw no clinically significant changes in QTc.

"The side effect profile is stellar," Dr. Prokocimer said. "When we increase the dose, we don't see a dose-related increase in the incidence of side effects."

He noted that unlike linezolid, the 200-mg dose of torezolid phosphate had virtually no effects on patients' laboratory values and showed no evidence of immunosuppression. The 200-mg dose will be the subject of two pivotal phase III studies, due to begin in 2010. ■