Ertapenem Effective for Diabetic Foot Infections

Once-daily ertapenem was as safe and effective as two other antibiotics given four times per day.

BY MITCHEL L. ZOLER
Philadelphia Bureau

WASHINGTON — Once-daily treatment with ertapenem was as safe and effective as a four-times daily regimen with two other antibiotics for treating diabetic patients with moderate to severe foot infections in a controlled study with 445 evaluable patients.

"This is the largest and most comprehensive randomized controlled trial of treatment of moderate to severe diabetic foot infection to date, and the only one with a double-blind design," Benjamin A. Lipsky, M.D., said while presenting a poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The study was sponsored by Merck, which markets ertapenem (Invanz).

The multicenter study enrolled adult men and women with diabetes and a moderate to severe foot infection that required 5-28 days of treatment with a parenteral antibiotic. Patients were randomized to intravenous treatment with either 1 g of ertapenem once daily, or 3.375 g of piperacillin plus tazobactam every 6 hours. Patients could continue on the intravenous regimen, if needed, for up to 28 days, but patients who were treated for at least 5 days and met certain clinical criteria for improvement were switched to an oral regimen with amoxicillin and clavulanate.

The study's primary outcome was the percent of patients who achieved a favorable response of cure or clinical improvement by the time their intravenous therapy was stopped. The study was designed to test whether ertapenem was not inferior to the comparator regimen.

Randomization placed 289 patients in the ertapenem group and 287 in the piperacillin plus tazobactam group. For the primary end point, 226 patients were evaluable in the ertapenem group and 94.2% had a favorable response by the time their intravenous treatment stopped, compared with a 92.2% response rate among the 219 evaluable patients in the comparator group, reported Dr. Lipsky, professor of medicine at the University of Washington, Seattle. The difference between the two groups was not statistically significant.

The two regimens also had identical effects when assessed by the study's secondary efficacy outcomes: the percentage of patients with a favorable response 10 days after antibiotic therapy was stopped, and the percentage of patients who had both a favorable clinical response and either microbiologic eradication or presumptive eradication by 10 days after treatment was stopped.

The safety profiles of the two regimens also were very similar. The fraction of patients with one or more adverse events was identical in both groups, 47.4%, and the fraction with serious, drug-related adverse events was also identical, 0.3%, Dr. Lipsky reported at the conference, which was sponsored by the American Society for Microbiology.

The fraction of patients who stopped therapy because of drug-related adverse events was 1.0% in the ertapenem group and 2.1% in the piperacillin plus tazobactam group. The most common adverse events in both groups were diarrhea, nausea, and headache, although diarrhea was more common among patients treated with piperacillin plus tazobactam. ■

Fatal Infection in a Lupus Patient Shows Delicate Balance in Treatment

BY NANCY WALSH
New York Bureau

BUDAPEST, HUNGARY — The death of a patient with lupus from disseminated cryptococcosis illustrates the difficulty in finding the balance between therapeutic immunosuppression and treatment of a resulting infectious disease, Dr. Gabor Szabad said at an international symposium sponsored by the European Academy of Dermatology and Venereology.

The patient was a 36-year-old woman who had been diagnosed with systemic lupus erythematosus in 1989 when she began experiencing muscle weakness, fever, and arthropathy and also developed the characteristic facial butterfly rash. She was antinuclear antibody positive, and double-stranded DNA antibodies were present.

During the subsequent decade, she developed lupus nephritis, cerebral lupus, lower extremity ulceration, and Raynaud's phenomenon–associated gangrene that necessitated the amputation of two fingers, Dr. Szabad said.

Throughout these years, she was receiving continuous immunosuppressive therapy with prednisolone, cyclophosphamide, and azathioprine in varying doses.

In 2002, she presented with reddish-brown infiltrates across the gluteal area and yellowish nodules and papules on the left hand. She had an elevated sedimentation rate, marked lymphopenia, and mild renal insufficiency; a thoracic CT scan showed evidence of pneumonia, said Dr. Szabad of the department of dermatology and allergology, University of Szeged (Hungary).

Histopathologic investigation of the skin lesions revealed the presence of yeastlike organisms in the dermis. Buff-colored mucoid colonies characteristic of the genus *Cryptococcus* grew on culture and were positive on a cryptococcal antigen latex agglutination test.

Subsequent efforts to manipulate antimycotic, antibiotic, and immunosuppressive therapies resulted in a seesaw course. She died of acute respiratory distress syndrome on day 51.

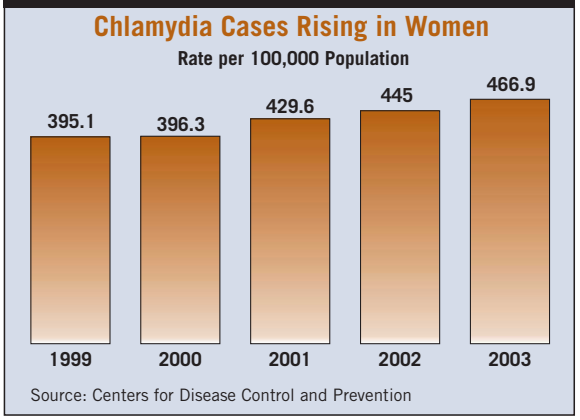
Autopsy findings included mesangial glomerulonephritis, pulmonary cryptococcosis, and cryptococcal epidermolysis, Dr. Szabad said.

Most cases of disseminated cryptococcosis occur in patients who are immunocompromised because they have AIDS or received an organ transplant.

"Lupus patients also are susceptible to opportunistic infections such as this because of their prolonged immunosuppressive therapy, but the intrinsic immunologic abnormalities of systemic lupus erythematosus can also contribute to the susceptibility," he said.

Most cases of serious cryptococcal infection in patients with lupus manifest as meningeal disease. The first reported case of cutaneous cryptococcosis in a patient with underlying lupus involved a 24-year-old woman who presented with cellulitis of the thigh and gluteus and who went on to develop nephrotic syndrome, arterial hypertension, and ultimately fatal acute renal insufficiency (Mycoses 2001; 44:419-21). ■

DATA WATCH



KEVIN FOLEY, RESEARCH

CDC Web Site Offers Malaria Telediagnosis, Tx Guidelines

BY DAMIAN MCNAMARA
Miami Bureau

MIAMI BEACH, FLA. — Want to confirm a suspected case of malaria?

You can e-mail a digital image to the Centers for Disease Control and Prevention for telediagnosis.

Then, if your patient requires treatment for malaria, you can download guidelines for treatment from its new malaria Web site, Phuc Nguyen-Dinh, M.D., said at the annual meeting of the American Society of Tropical Medicine & Hygiene.

In less than 1 year, the CDC's online malaria initiative (www.cdc.gov/malaria) has supplanted many calls to the center's malaria hotline.

Because malaria is relatively rare in the United States, with an estimated 1,200 cases identified per year, clinicians often need assistance in making the diagnosis and deciding on the treatment.

To that end, the CDC offers malaria publications, diagnostic reference services, and training seminars for laboratory personnel.

"Now information is downloadable from the Web site. We believe it is more accurate to print the guidelines than to get information over the telephone. Plus, with the Web site we can update the information as needed," said Dr. Nguyen-Dinh, medical officer in the division of parasitic diseases at the Centers for Disease Control and Prevention, Atlanta.

The response to the Web site has been positive, Dr. Nguyen-Dinh said. The clinical guidelines are especially useful, according to 430 physicians surveyed through the Infectious Diseases Society of America's Emerging Infections Network.

The Web site features prevention information, with a link to the CDC's travelers' information site. It also features interactive training for recognition of malaria, including a quiz, sample images, and case studies.

"We know there is a need in the United States for better diagnosis," said Stephanie Johnson, who is a CDC researcher in the Division of Parasitic Diseases.

In 2002-2003, the CDC received 188 requests for telediagnosis, of which 79 were for suspected malaria. If the telediagnosis is malaria, the CDC requests the sender submit samples for verification.

Health care providers can e-mail images of other suspected parasitic infections to the CDC's Laboratory Identification of Parasites of Public Health Concern program (www.dpd.cdc.gov/dpdx). ■

The Centers for Disease Control and Prevention's malaria hotline, 770-488-7788, operates Monday through Friday, 8 a.m. to 4:30 p.m. EST; the after-hours emergency number is 770-488-7100.