Iclaprim Comparable to Linezolid for Skin Infection

BY KERRI WACHTER
Senior Writer

WASHINGTON — The novel antibiotic iclaprim appears to be comparable to linezolid in terms of safety and efficacy in the treatment of complicated skin and skin structure infections, based on the results of a study of almost 1,000 patients.

The clinical cure rate for the intent-to-treat (ITT) population was 82% for those on iclaprim, compared with 85% for those on linezolid (Zyvox), Dr. Maria Solonets reported in a poster presented at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the annual meeting of the Infectious Diseases Society of America (IDSA).

"Based on the clinical experience to date, iclaprim appears to be a safe and effective potential alternative for the treatment of complicated skin and skin structure infections, including those caused by MRSA [methicillin-resistant *Staphylococcus aureus*] and group A streptococcus," Dr. Solonets and her coinvestigators wrote.

Iclaprim is an investigational broad-spectrum diaminopyrimidine that has shown potent in vivo activity against predominantly gram-positive pathogens that are associated with complicated skin and skin structure infections. Dr. Solonets and several of her coinvestigators are employed by Arpida Ltd., Reinach, Switzerland, which is developing the drug.

The data come from the combined results of two Arpida-sponsored phase III clinical trials (ASSIST-1 and ASSIST-2). For both studies, patients (18 years or older) with complicated skin and skin structure infections with a minimum of three local and one systemic sign or symptom of infection were enrolled. Patients were randomized to either 0.8 mg/kg iclaprim infused over a period of 30 minutes every 12 hours or 600 mg linezolid infused over 30 minutes every 12 hours.

Patients were allowed concomitant use of aztreonam and metronidazole for the treatment of gram-negative organisms in mixed infections. However other systemic or topical antibiotics, steroids, or class Ia/III antiarrhythmic drugs were prohibited.

The intent-to-treat population included all randomized patients who received at least one dose of the study medication. The modified intent-to-treat population included all patients in the ITT population who had an infecting gram-positive pathogen isolated at baseline.

Clinical cure was determined by the resolution of signs and symptoms of infection present at baseline or by clinically relevant improvement of local or systemic signs and symptoms of infection. Patients evaluated for clinical cure had to have a minimum of 4 days of treatment and at least seven doses of the study drug. The ITT population included 500 patients randomized to iclaprim and 491 patients randomized to linezolid. Most patients in both groups—92% in the iclaprim and 93% in the linezolid group—were categorized with severe infection.

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The most common infection type was deep or extensive cellulitis, followed by wound infections and major abscess. Microbiologic eradication or presumed eradication was based on the absence from any culture, at the test-of-cure assessment, of the causative pathogen isolated at baseline.

S. aureus was the most commonly isolated pathogen at baseline—found in more than 75% in both treatment groups. Approximately 40% of *S. aureus* isolates were MRSA. MRSA eradication rates for iclaprim were similar to those for linezolid—76% and 79%, respectively.

In terms of safety, the number of adverse events possibly or probably due to the study drug was comparable for iclaprim (113) and linezolid (137). The most common adverse events were gastrointestinal disorders.

Arpida Ltd. announced that it has received notice from the Food and Drug Administration that the agency's Anti-Infective Drugs Advisory Committee will discuss the new drug application (NDA) for intravenous iclaprim in complicated skin and skin structure infections. ■