Ceftaroline Found Effective for Skin Infections

BY KERRI WACHTER
Senior Writer

WASHINGTON — The investigational antibiotic ceftaroline was found to be effective against a range of gram-positive and gram-negative organisms that can cause complicated skin and skin structure infections, according to data from a phase III noninferiority study of more than 600 patients.

Clinical cure rates (8-15 days after therapy ended) were similar for patients who received at least one dose of ceftaroline or vancomycin/aztreonam (the modified intent-to-treat population)—87% for those on ceftaroline and 86% with vancomycin-aztreonam, according to data from the CANVAS-1 study presented as a poster at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

"Ceftaroline monotherapy was as effective and well tolerated as vancomycin plus aztreonam combination therapy in treating patients with complicated skin and skin structure infections due to both gram-positive and gram-negative pathogens," wrote Dr. Ralph Corey of Duke University, Durham, N.C., and his coinvestigators. The study was supported by Forrest Laboratories Inc., which is developing ceftaroline. Two of Dr. Corey's coinvestigators are employed by Cerexa Inc., which is a wholly-owned subsidiary of Forest. Dr. Corey disclosed having received research funding and serving as an adviser to Cerexa.

The randomized, double-blind study enrolled adults with local and systemic evidence of complicated skin and skin structure infections. Patients were randomized to either 600 mg intravenous ceftaroline every 12 hours for 5-14 days or 1 g intravenous vancomycin plus 1 g intravenous aztreonam (Azactam) every 12 hours for 5-14 days. Aztreonam was discontinued if gram-negative pathogens were not identified or suspected.

At enrollment, 353 patients were randomized to receive ceftaroline and 349 were randomized to receive vancomycin/aztreonam. The modified intention-to-treat population included all patients who had received any study drug—351 patients in the ceftaroline group and 347 patients in the vancomycin/aztreonam group.

Almost a quarter of the patients in each group had polymicrobial infection. The most common infection type was deep, extensive cellulitis (35% in both groups), followed by major abscess (28% of the ceftaroline group and 29% of the vancomycin/aztreonam group).

There were 471 patients—244 in the ceftaroline group and 227 in the vancomycin/aztreonam group—who were microbiologically evaluable. Microbiologic eradication was achieved in 92% of patients on ceftaroline and 93% of patients on vancomycin/aztreonam.

Staphylococcus aureus was the most commonly isolated organism, but ceftaroline was effective against a range of gram-positive and gram-negative organisms. (See table.)

Most adverse events were mild. The most common adverse events with ceftaroline were nausea (6%) and headache (5%). The most common adverse event in the vancomycin/aztreonam group was pruritus (8%), followed by nausea and generalized pruritus (5% each). ■

Clinical Cure/Microbiological Eradication by Organism

	Clinical Cure		Microbiological Eradication	
	Ceftaroline	Vanco/Az	Ceftaroline	Vanco/Az
Gram-positive				
Staphylococcus aureus	93%	95%	94%	92%
MRSA	95%	95%	95%	92%
MSSA	91%	95%	93%	93%
Streptococcus pyogenes	100%	100%	100%	100%
Streptococcus agalactiae	93%	100%	86%	100%
Enterococcus faecalis	93%	92%	93%	92%
Gram-negative				
Escherichia coli	90%	87%	90%	87%
Klebsiella pneumoniae	91%	100%	91%	100%
Proteus mirabilis	70%	90%	80%	90%
Pseudomonas aeruginosa	100%	90%	89%	90%

Note: Based on a study of 244 patients who received ceftaroline and 227 who received vancomycin/aztreonam (vanco/az).
Source: Dr. Corey

ELSEVIER GLOBAL MEDICAL NEWS

First in New Class of Antibiotics Compares Well With Linezolid

BY KERRI WACHTER
Senior Writer

WASHINGTON — The investigative antibiotic PTK 0796 appears to be comparable to linezolid in terms of efficacy against skin and skin structure infections and safety, based on the results of a phase II study of more than 200 patients.

Clinical success for the intention-to-treat population (those randomized, who received at least one dose) was 88% for the PTK 0796 group and 76% for the linezolid group, according to a poster presented at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Clinical success was defined as the blinded evaluator's assessment that the infection was sufficiently resolved, such that no additional antibiotic therapy was required, at the test-of-cure visit. Patients who were not evaluated at a test-of-cure visit were considered clinical failures.

PTK 0796 is the first of a new class of antibiotics—the aminomethylcyclines—which are semisynthetic compounds that are related to tetracycline. The drug is being developed by Paratek Pharmaceuticals, which carried out the study.

Patients with complicated skin and skin structure infections were randomized to receive either intravenous PTK 0796 or linezolid (Zyvox) and could be switched to oral therapy at the investigator's discretion. Intravenous dosing was 100 mg PTK 0796 every 24 hours or 600 mg linezolid every 12 hours. Oral dosing was 200 mg PTK 0796 every 24 hours or 600 mg linezolid every 12 hours. If the investigator considered that a patient might require gram-negative coverage, patients on linezolid could receive aztreonam (Azactam) infusions and those on PTK 0796 could receive placebo infusions.

In all, 118 patients were randomized to receive PTK 0796 and 116 patients, to linezolid. Patients in both groups were similar in terms of demographics, type of infection, severity of infection, and comorbidities. Major abscesses were the most common type of infection in both groups—73 patients in the PTK 0796 group and 72 in the linezolid group.

Duration of treatment was similar for both groups. Intravenous duration was 4 days for the PTK 0976 group and 3 days for the linezolid group. Overall antibiotic duration was 10 days for both the PTK 0796 and linezolid groups.

In terms of microbiology, the primary pathogen was known for 84 patients in the PTK 0796 group and for 78 patients in the linezolid group. MRSA was the most common primary pathogen isolated in both the PTK 0796 and linezolid group—52% and 49%, respectively. Clinical efficacy against MRSA was 96% in the PTK 0796 group and 79% in the linezolid group.

There were no drug-related serious adverse events in either group. No patient discontinued PTK 0796 because of adverse events, compared with two patients in the linezolid group. The most common adverse events in both groups were gastrointestinal—21 in the PTK 0796 group and 18 in the linezolid group. ■

A Missing Diagnosis May Call for Empiric Treatment

BY SHARON WORCESTER
Southeast Bureau

DESTIN, FLA. — Don't be afraid to treat infections empirically in patients in whom you have no definitive diagnosis, if you have considered the differential diagnoses and have ruled out more ominous conditions, Dr. Bari Cunningham said.

"It's okay—and at times, necessary—to treat empirically," said Dr. Cunningham at a meeting sponsored by the Alabama Dermatology Society.

She described the case of a gardener who presented with what appeared to be severe acne on his back. Various acne washes and medications failed to resolve the acne.

The patient's job involved carrying burlap sacks of branches and sticks; he typically carried the bags over his shoulders and slung across his back, said Dr. Cunningham, who assumed the "acne" was actually some kind of inoculation injury.

Various diagnoses were considered, including mycetoma, sporotrichosis, deep fungal infection, and foreign body reactions. Various studies showed granulomas and suppurative inflammation, but they were negative for these differential diagnoses.

Without a diagnosis, Dr. Cunningham, a pediatric dermatologist at the University of California, San Diego, decided to treat empirically after the patient returned complaining of tenderness and extensive drainage from the lesions. The patient was successfully treated with trimethoprim/sulfamethoxazole, clarithromycin, and ciprofloxacin.

"He ultimately completely cleared," she said. The outcome underscores the fact that it is, indeed, okay to treat empirically.

"I really, in retrospect, should have started him right away and not made him wait 4 or 5 months," she said. "I had the pathology—I had everything. There was no reason why I shouldn't have just treated empirically right off the bat." ■