# *New Fluoroquinolone for Community-Acquired Pneumonia Is Promising*

BY SHERRY BOSCHERT
*San Francisco Bureau*

SAN FRANCISCO — An experimental fluoroquinolone compared favorably with amoxicillin or ceftriaxone for the treatment of community-acquired pneumonia in separate randomized, double-blind phase III trials, investigators reported in poster presentations at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

One study of 308 outpatients in Europe and Russia with mild to moderate community-acquired pneumonia showed similar response rates in patients given 5 days of oral garenoxacin or 10 days of oral amoxicillin, reported Dr. Hetty Waskin of Schering-Plough Research Institute, Kenilworth, N.J. The company is developing garenoxacin and funded the study. The lead investigator in the study was Dr. N. Mogulkoc of Ege University, Izmir, Turkey.

Evaluations that were conducted 7-14 days after completing therapy showed clinical responses in 91% of patients randomized to once-daily doses of 400 mg garenoxacin and in 87% of patients given amoxicillin 1 g t.i.d. The drugs eradicated pneumonia bacteria in 88% of the garenoxacin group and 91% of the amoxicillin group.

Drug-related adverse events—most commonly diarrhea, headache, abdominal pain, and nausea—were seen in 13% of patients in the garenoxacin group and 12% of those in the amoxicillin group.

The second study of 406 hospitalized patients with community-acquired pneumonia showed an 88% clinical cure rate in 328 evaluable patients regardless of treatment group. Patients were randomized to receive either IV garenoxacin 400 mg/day with possible step-down to oral garenoxacin 400 mg/day or IV ceftriaxone 1-2 g/day with possible step-down to oral clarithromycin 500 mg b.i.d. If clinicians suspected atypical pneumonia, patients in the ceftriaxone group also could receive IV erythromycin 0.5-1 g every 6 hours.

Patients were treated for 7-14 days and evaluated for cure 7-14 days after completing therapy, said Dr. Mark E. Dowell of Casper, Wyo., the study's primary investigator. He has no other relationship with Schering-Plough except that the company funded the study and a company employee (Dr. Waskin) was a coinvestigator.

Bacterial eradication rates were 86% for the garenoxacin group and 89% for the ceftriaxone group.

Schering-Plough hopes to win European approval for the drug for community-acquired pneumonia in 2007, but will be looking for a marketing partner to pursue approval of the drug in the United States, Dr. Waskin said.

The conference was sponsored by the American Society for Microbiology. ■

# Noncompliance With Antibiotic Guideline for CAP May Up Costs

BY BRUCE JANCIN
*Denver Bureau*

SALT LAKE CITY — Failure to prescribe antibiotics in accordance with current guidelines for the treatment of severe community-acquired pneumonia comes at an average cost of 3 extra days on mechanical ventilation, Dr. Andrew F. Shoor reported at the annual meeting of the American College of Chest Physicians.

Given a conservative estimated cost of $2,500 per day of mechanical ventilation, noncompliance with this guideline costs the health care system an average of $7,500 each time a patient with severe community-acquired pneumonia (CAP) is prescribed an antibiotic regimen other than one of those recommended in Infectious Diseases Society of America (IDSA) guidelines. That makes the rate of compliance with the IDSA guidelines a quality assurance yardstick worth measuring, said Dr. Shoor, associate director of pulmonary and critical care medicine at the Washington (D.C.) Hospital Center. He reported on 199 patients requiring mechanical ventilation for severe CAP who participated in a multicenter prospective registry. Of these, 40% received antibiotics not in accord with IDSA guidelines.

After controlling for numerous potential confounding variables—including comorbid illnesses, patient demographics, time to initiation of antibiotics, pathogen, disease severity, and corticosteroid therapy—the use of an antibiotic regimen that was not in accord with IDSA recommendations was associated with 3 extra days on mechanical ventilation. The only other independent predictor of increased duration of mechanical ventilation was the development of acute renal failure.

"The purpose of this study was to ask, 'Is there any value, in terms of resource use, to compliance with the guidelines?' If this [analysis] had shown there was no value to compliance, then making all these guidelines is foolish, and we should be focusing instead on other health care issues," Dr. Shoor said.

**'The rate of compliance matters. We can do things better and save money.'**

**DR. SHOOR**

"But these results suggest that while I may not be able to show cause and effect, the signal is definitely going the wrong way," he added. "This impact is clearly detrimental and it's clearly independent of multiple confounders. It shows the rate of compliance matters. We can do things better and save money."

Critical care specialists have much to learn from cardiologists with regard to performance measurement, he said. When quality improvement programs measure the percentage of a physician's patients who are prescribed a β-blocker after a myocardial infarction, for example, this is done based on good evidence that the therapy reduces cardiovascular morbidity and mortality.

"We haven't done that very well in critical care. We have a host of guidelines—sepsis, ventilator-assisted pneumonia, community-acquired pneumonia—but we haven't made the effort yet to see if whether we use them or not affects outcomes. And I think we have to," he said.

He readily conceded that the association between noncompliance with the IDSA guideline and the lengthier mechanical ventilation identified in his study doesn't prove causality. That would require a randomized trial. And for ethical reasons, there will never be a trial in which some critically ill participants are randomized to guideline-noncompliant antibiotic treatment. An observational study with rigorous attempts to control for potential confounders, such as this one, is a practical alternative, he said.

An intriguing finding in this study, Dr. Shoor noted, is that the actual adequacy of antibiotic therapy, as demonstrated by bacterial culture results, didn't differ between the IDSA guideline–compliant and –noncompliant patient groups. Thus, the precise mechanism by which guideline noncompliance results in more time on the mechanical ventilator remains unclear. "You might think that IDSA guideline compliance works by increasing the initial adequacy of antibiotics, but that didn't seem to be the case." ■

# Tigecycline on Horizon for Community-Acquired Pneumonia

BY SHERRY BOSCHERT
*San Francisco Bureau*

SAN FRANCISCO — Tigecycline appeared to be comparable in efficacy and tolerability to levofloxacin in treating community-acquired pneumonia in two phase III studies of 891 hospitalized patients needing intravenous therapy, Dr. Gary Dukart reported in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

If approved, tigecycline would be the first glycylcycline available to treat pneumonia, said Dr. Dukart of Wyeth Research, Collegeville, Pa., and his associates. Wyeth markets the drug, which is approved in 40 countries including the United States for the treatment of complicated intra-abdominal infections and complicated skin and skin structure infections. Tigecycline is a broad-spectrum antibiotic with in vitro activity against gram-positive, gram-negative, anaerobic, and atypical bacteria, including some resistant strains.

A separate study of tigecycline therapy for hospital-acquired pneumonia is ongoing. Once that is complete, the company plans to apply in 2007 for approval of tigecycline to treat community- or hospital-acquired pneumonias, he said.

Patients in the multicenter, double-blind studies of community-acquired pneumonia were randomized to 7-10 days of treatment with intravenous tigecycline (100 mg initially, then 50 mg every 12 hours) or intravenous levofloxacin. Dosages of levofloxacin differed between the two trials. In one, patients received 500 mg every 24 hours. In the other, they got 500 mg every 12 or 24 hours at the discretion of the physician and based on local practice. In one trial, patients who showed improvements in their signs and symptoms of pneumonia could be switched after at least 3 days of intravenous therapy to oral levofloxacin for the duration of therapy.

The mean duration of treatment in both groups was 10 days. The mean hospital stay in both groups was 6 days.

Among 846 patients who received at least one dose of medication (a modified intent-to-treat population), 81% on tigecycline and 80% on levofloxacin were considered cured. Among 574 "evaluable" patients who were assessed for cure between 7 and 23 days after the last dose of medication, 90% in the tigecycline group and 86% in the levofloxacin group were cured. The differences between groups were not significant.

Among 40 patients with pneumonia due to documented *Streptococcus pneumoniae* infection, tigecycline cured 20 (91%) of 22 patients and levofloxacin cured 13 (72%) of 18. The rate of discontinuing medication because of side effects did not differ significantly between groups—6% with tigecycline and 8% with levofloxacin. Serious adverse events occurred in 10% with tigecycline and 11% with levofloxacin. In each group, 3% of patients died, but the deaths were not considered related to the medications.

Drug-related adverse events affected 48% on tigecycline and 37% on levofloxacin, a significant difference. A significantly greater proportion of patients in the tigecycline group experienced nausea or vomiting (24% and 16%, respectively), compared with the levofloxacin group (6% and 3%). Patients in the tigecycline group were significantly less likely to have elevated ALT or AST levels (3% and 2%), compared with the levofloxacin group (6% and 6%). Other common side effects were comparable between groups.

The conference was sponsored by the American Society for Microbiology. ■