Resistance Can Torpedo Treatment With Macrolides

BY SHERRY BOSCHERT
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SAN FRANCISCO — Drug resistance was a common cause of treatment failure in 26 patients with community-acquired pneumonia who developed bacteremia while being treated with macrolide antibiotics, Dr. Gavin Bayan Grant said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Of the 26 patients who developed bacteremia while on erythromycin, clarithromycin, or azithromycin therapy, 21 (81%) had resistant organisms, compared with 15 (44%) of 34 patients who developed bacteremia after recent use of one of the macrolides (defined as 16-90 days before the bacteremia diagnosis) and 14% of 721 patients who had not been taking any antibiotics and developed bacteremia.

Macrolide antibiotics are standard therapy for outpatient treatment of pneumonia, and evidence that significant macrolide resistance occurs has been inconclusive, said Dr. Grant of the Centers for Disease Control and Prevention, Atlanta. The current findings provide further evidence that resistance can lead to treatment failure with macrolides, which may inform clinical decisions to change antibiotics in some patients, he said at the meeting, sponsored by the American Society for Microbiology.

Dr. Grant has no association with the companies that make macrolides.

After controlling for patient age, immunosuppression, chronic comorbidities, and residence in a long-term care facility, patients failing macrolide therapy were 5 times more likely to have resistant organisms, compared with patients who developed bacteremia after recent macrolide use, and 26 times more likely to have resistance than patients with bacteremia who had not been taking antibiotics.

The study also found that clinicians who define macrolide resistance using a cutoff of a minimum inhibitory concentration (MIC) of at least 16 mcg/mL will miss a significant percentage of the treatment failures. "Failures often occur at macrolide MICs less than 16 mcg/mL," he said. ■

Garenoxacin Shows Promise for Community-Acquired Pneumonia

BY SHERRY BOSCHERT
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SAN FRANCISCO — An experimental fluoroquinolone compared favorably with amoxicillin or ceftriaxone for treating community-acquired pneumonia in two phase III trials, researchers 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 (CAP) 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 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. Bacterial eradication was achieved 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 CAP showed an 88% clinical cure rate in 328 evaluable patients regardless of treatment group. Patients were randomized to 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 atypical pneumonia was suspected, the ceftriaxone patients 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 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. ■