Telithromycin Targets Respiratory Pathogens

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — Telithromycin is an excellent first-line choice for empiric outpatient treatment of mild-to-moderate respiratory tract infections, Carman A. Ciervo, D.O., declared at a satellite symposium held in conjunction with Wonca 2004, the conference of the World Organization of Family Doctors.

The drug, first in the novel ketolide class of antibiotics, has well-established efficacy against the full spectrum of respiratory tract pathogens: the typical and atypical ones, as well as resistant strains. Most importantly, it provides a tailored spectrum of coverage, sparing the primarily enteric gram-negative pathogens such as *Escherichia coli* and *Proteus mirabilis*. This will minimize emergence of resistance among the gram-negatives that cause important GI and urinary tract infections, explained Dr. Ciervo, chairman of the department of family medicine at the University of Medicine and Dentistry of New Jersey School of Osteopathic Medicine, Stratford.

I think the advantage that the ketolides have is that they are a judicious way to treat respiratory tract infections.

DR. CIERVO

"I think the advantage that the ketolides have, similar to what the macrolides had in the early '90s, is that they really are a judicious way to prescribe to treat a respiratory tract infection. They cover the bugs that you need to cover for a respiratory tract infection, including the resistant organisms. [However,] I wouldn't be prescribing drugs in this class if I was concerned about diverticulitis or a urinary tract infection, but for the respiratory tract telithromycin is certainly a good choice," added Dr. Ciervo, who is on the speakers' bureau for Aventis, which sponsored the symposium.

Collateral damage to gram-negative pathogens is a significant problem with the fluoroquinolones, with their broad spectrum. It's for this reason that the Centers for Disease Control and Prevention recommends against using the newer fluoroquinolones as first-line therapy in community-acquired pneumonia.

"Better that we reserve them for when we really need them to cover the gram-negatives. When you're treating a respiratory tract infection, why not prescribe an antibiotic that's tailored for patients with respiratory tract infections? That way we can impact future resistance rates of GI tract and urinary pathogens," he continued.

The fluoroquinolones and ketolides share a property that imparts a low propensity to develop resistance: dual binding to the bacterial ribosome. Alteration of the ribosomal binding site is an important mechanism by which bacteria become resistant to antibiotics. This is less likely to occur when a drug has two binding sites.

Unlike the fluoroquinolones, macrolides, another often-prescribed drug class for respiratory tract infections, don't cause collateral damage to gram-negative pathogens. But they don't cover the full spectrum of respiratory tract pathogens. Macrolides have poor activity against penicillin-nonsusceptible *Streptococcus pneumoniae*, and the incidence of such infections in the United States has been on a steady rise since the mid-1990s.

Macrolide-resistant *S. pneumoniae* is also an emerging problem. It appears to be promoted by use of macrolides having a very long half-life. Azithromycin, for example, has a 72-hour half-life and, consequently, a high potential to select for resistance due to prolonged exposure to subtherapeutic drug concentrations. Telithromycin, in contrast, has a 10-hour half-life.

Telithromycin features once-daily dosing and a 5-day treatment course. There is a growing appreciation that patient compliance falls off dramatically with dosing more than once daily or for more than 5 days, Dr. Ciervo said.

In response to a question, he described doxycycline as "an important and underutilized option" for respiratory tract infections in younger patients—say, those aged 15-50 years—without comorbidity or other significant risk factors for resistant infection, such as having children in day care, chronic renal insufficiency, or recent history of beta-lactam therapy. ■

Pages 30a—30b