

Infectious Diseases Pipeline

By Alice Goodman

A few drugs in development were featured at the Infectious Diseases Society of America (IDSA) 2009 annual meeting. Infectious disease (ID) experts warn that the ID pipeline is dying, with only few drugs currently in development. Yet, the threat of new infections is growing worldwide in the inpatient and outpatient settings.

Oritavancin is a semisynthetic lipoglycopeptide, with potent activity against multidrug-resistant gram-positive pathogens. The drug has undergone phase 3 clinical trials for skin and skin-structure infections and is currently under review by the Food and Drug Administration (FDA). A study presented at IDSA showed that oritavancin was 8 times more active than daptomycin and between 16 and 32 times more active than vancomycin and linezolid against methicillin-resistant staphylococci. Oritavancin was the most potent of the tested drugs in subsets of gram-positive organisms, regardless of resistance phenotype. Oritavancin holds promise for the treatment of serious infections caused by gram-positive pathogens.

Telavancin. After a lengthy struggle, the FDA approved telavancin (Vibativ) in September 2009 for adults with complicated skin and skin-structure infections caused by susceptible gram-positive bacteria, including *Staphylococcus aureus*, both methicillin-resistant *S aureus* (MRSA) and methicillin-susceptible strains. Telavancin is a bactericidal, once-daily injectable lipoglycopeptide antibiotic.

A poster presented at IDSA 2009 showed the potent activity of telavancin against gram-positive isolates cultured from skin and skin-structure infections, including *S aureus*, and its superior potency against MRSA compared with vancomycin, daptomycin, linezolid, and quinupristin/dalfopristin.

CEM-102 is an investigational oral formulation of fusidic acid. Fusidic acid has been successful in treating staphylococcal infections (including MRSA) outside of the United States. This drug has a unique mechanism of action and low levels of bacterial resistance. At IDSA, 3 posters

confirmed CEM-102's potency against current isolates of *S aureus*, including MRSA. Isolates resistant to other antibiotics were susceptible to CEM-102, indicating little cross resistance to CEM-102. In 1 poster, 3 different testing methods confirmed susceptibility to CEM-102 across multiple *S aureus* strains. In a study presenting data from 69 healthy controls, a loading dose of CEM-102 1200 mg twice daily followed by 600 mg twice daily on subsequent days provides superior antibacterial effect compared with regimens without a loading dose.

CEM-102, Ceppra Pharmaceuticals' novel fluoroketolide antibiotic, has potent and broad-spectrum activity against gram-positive and gram-negative bacteria, including multidrug-resistant strains and nonbacterial pathogens such as *Plasmodium falciparum*. A study presented at IDSA showed that CEM-102 was effective against 1737 multidrug-resistant *S pneumoniae* strains collected in the United States, Europe, and Latin America. The drug is about to enter a phase 2 trial in moderate to moderately severe community-acquired bacterial pneumonia.

Intravenous Colistin is not a drug in the pipeline. However, it deserves mention because it has been resurrected after 50 years of relative obscurity. The use of this drug has increased rapidly in the past 3 years as a last-resort treatment for the growing number of multidrug-resistant gram-negative bacterial infections. There are no good studies on the best way to use intravenous Colistin. A study presented at IDSA focused on 33 critically ill older patients with 37 multidrug-resistant *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* infections. Clinical and microbiologic cure rates were 81% and 34%, respectively. In 8 of 10 patients who developed nephrotoxicity, overdosing based on body weight appeared to be the culprit. The investigators suggest that using ideal body weight instead of actual body weight may be a safer way to dose this drug to avoid nephrotoxicity, especially in overweight or obese patients. ■