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ICAAC/IDSA Symposium Highlights Alternatives to Vancomycin

Vancomycin — usually used as a drug of last resort to treat infections caused by gram-positive bacteria — is increasingly being replaced by other agents because of the emergence of vancomycin-resistant organisms. Speakers at the 48th Annual ICAAC/ IDSA 46th Annual Meeting last month in Washington, D.C., talked about newer and investigational alternative agents, which may be used alone or in combination with vancomycin.

Daptomycin is useful against skin and soft-tissue infections, according to David Snyderman, MD, of Tufts Medical Center in Boston. It is effective for the treatment of *Staphylococcus aureus* bacteremia (including MRSA), *Streptococcus pyogenes*, and endocarditis. There is promising data to support the use for vancomycin-resistant enterococcus (VRE) bacteremia and osteomyelitis. The drug is not indicated for pneumonia and should not be used for pulmonary infections.

Toxicity is not a major issue, Dr. Snyderman said, but physicians should monitor creatine phosphokinase at all dosages, especially higher ones. The dosage can be as high as 10 mg/kg for 4 days instead of the standard 4 mg/kg for 8 days for skin and soft tissue infections, he suggested. Clinicians should be vigilant for resistance; there is documented emergence of resistance with *S. aureus* and VRE. Daptomycin can be used with other agents, but synergy is hard to predict. Data support the coadministration of rifampin, Dr. Snyderman said, but use caution when administering with tobramycin. There are no drug interactions between daptomycin and the cytochrome P450 system.

Linezolid is indicated for skin infections (including MRSA) and pneumonia. It may be superior to vancomycin for ventilator-associated pneumonia (especially when caused by MRSA), according to Dilip Nathwani, MD, of the Ninewells Hospital Medical School in Dundee, Scotland. Recruitment is ongoing for a study of nosocomial pneumonia with suspected or proven MRSA. Dr. Nathwani also presented data showing linezolid performed better than vancomycin in treating complicated skin and skin structure infections.

Tigecycline is the first glycylcycline (a tetracycline analogue) agent; it has excellent in-vitro efficacy against gram-positive infections, said Yehuda Carmeli, MD, of the Tel Aviv Sourasky Medical Center in Israel. No resistance has been encountered yet, making tigecycline a good alternative to vancomycin in certain instances, Dr. Carmeli

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said. The agent is active against MRSA, VRE, and other gram-positive infections, some gram-negative ones (but not *Pseudomonas* and *Proteus*). Tigecycline is approved for soft-tissue infections and intra-abdominal infections and has been tested in pneumonia, but a comparative trial failed to show non-inferiority. The manufacturer withdrew application for a community-acquired pneumonia indication. Dr. Carmeli urged clinicians to use caution when using to treat sites not yet well studied, particularly lung infection.

Fusidic Acid can be a valuable adjunct for the treatment of serious *Staphylococcus* infections, said John D. Turnidge, MD, of Women's and Children's Hospital in North Adelaide, Australia. Fusidic acid is still used widely in many countries as a topical (e.g., for impetigo and pyoderma). Resistance for these indications has emerged and spread in Europe. Activity is largely retained against MRSA, though an optimal dosage has not been established. Oral or parenteral fusidic acid should always be used in combination with another agent for the treatment of MRSA, Dr. Turnidge said. Experts have expressed concern that fusidic acid should not be used for minor infections but instead reserved for MRSA. Limitations of fusidic acid include GI intolerance and a lack of major controlled prospective studies for serious infections.

Although these drugs represent two different classes, **ceftobiprole** and **ceftaroline** are both active against MRSA, gram-positive infections, and gram-negative infections. Both are being studied for soft-tissue infections, said David C. Hooper, MD, of Massachusetts General Hospital in Boston. Ceftobiprole is also being studied for treatment of pneumonia.

Investigational Glycopeptides differ from vancomycin in several respects. According to Dr. George M. Eliopoulos, MD, of the Beth Israel Deaconess Medical Center in Boston, they offer greater potency in vitro and less frequent dosing. Clinical positioning of these investigational agents (described below) with respect to vancomycin remains to be determined upon the approval of these drugs.

- **Dalbavancin** shows promise for complicated skin and skin structure infections, including MRSA, but worldwide new drug applications were withdrawn in September. Additional Phase III multi-center studies are planned to provide additional data to support approval.
- **Telavancin** also is being investigated for complicated skin and skin structure infections. In two trials of more than 1,800 patients, telavancin at 10 mg/kg once daily was marginally superior to vancomycin 1g every 12 hours. However, the drug was more promising for MRSA, where telavancin successfully treated the infection in 91 percent of patients versus 86 percent of those receiving vancomycin. Serious adverse events were more common with telavancin in this study, however (7 percent versus 4 percent).
- **Oritavancin** has similar efficacy to vancomycin for the treatment of complicated skin and skin structure infections.

The pending approvals of telavancin and oritavancin in addition to the newer antibiotics expand physicians' treatment options for gram-positive drug-resistant organisms. However, as IDSA and others have pointed out, there is still a pressing need for new compounds that are active against multi-resistant, gram-negative organisms.

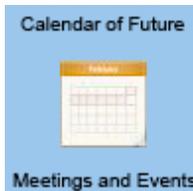
Antivirals for Pandemic Flu

Education and Resources

- Seasonal and Pandemic Influenza 2008 Monograph Now Available
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Note: IDSA and the American Society of Health-System Pharmacists are developing new clinical practice guidelines on vancomycin, which will be available early next year.

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