tion was 40 years. Two-thirds were male. The mortality rate was 4.4%.

Pneumonia was a complication of trauma in 1.6% of cases, acute respiratory distress syndrome (ARDS) in 0.5%, and bacteremia in 0.13%, said Dr. McClung, an emergency physician at Los Angeles County–USC Medical Center, Los Angeles.

The risks of pneumonia, bacteremia, and ARDS rose with each decade of age in a multivariate logistic regression analysis adjusted for potential confounders including age, sex, injury severity score, trauma mechanism, and days on a ventilator. The 56,680 children aged 5-12 years served as the comparison group. (See box, page 14). ■

Panel Votes in Favor of MRSA Antimicrobial

BY ELIZABETH MECHCATIE
Senior Writer

COLLEGE PARK, MD. — Clinical trial data show that the antibiotic telavancin is safe and effective for treating complicated skin and skin-structure infections, including those caused by methicillin-resistant *Staphylococcus aureus*, the majority of a federal advisory panel agreed.

The Food and Drug Administration's anti-infective drugs advisory committee voted 21-5 regarding the safety and efficacy of telavancin, with those voting in favor saying that despite their concerns about nephrotoxicity, QT prolongation, and possible teratogenic effects associated with the drug, they believed these risks were manageable.

The panel voted 18-5, with 3 abstentions, that there could be clinical situations in which the benefits of telavancin in pregnant women would outweigh its risks. All but one panelist agreed that a risk management strategy was needed to prevent unintended use in pregnant women or in women of childbearing potential.

Theravance Inc., the drug's manufacturer, has developed a risk management plan designed to minimize pregnancy exposures, the risk of nephrotoxicity, and the risk related to QT prolongation, and has proposed that the drug not be used during pregnancy, unless the benefit to the patient outweighs the potential risks to the fetus. The plan also includes recommendations to adjust the dose based on creatinine clearance and to avoid the drug in patients with conditions such as congenital long QT syndrome and uncompensated heart failure.

"I voted 'yes,' because I think vancomycin is a dying drug, and I see vancomycin resistance all the time," said panelist Dr. W. Kemper Alston, who is at the University of Vermont, Burlington. Those voting "no" on the safety and efficacy question cited concerns about the association of the drug with more than one toxicity.

"Safety concerns in multiple systems, not just one, complicate risk management," said the acting panel chair, Dr. L. Barth Reller, professor of medicine and pathology, Duke University, Durham, N.C. The mechanism of action was not that different from vancomycin, he added, so it is unclear how much its use would affect the problem of increasing resistance.

The FDA usually follows the advice of its advisory panels, which is not binding. The proposed indication for telavancin is for the treatment of complicated skin and skin structure infections (cSSSI) caused by *Staphylococcus aureus* (including methicillin-resistant isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus anginosus* group, and *Enterococcus faecalis*.

Telavancin, a bactericidal lipoglycopeptide antibiotic that has bactericidal activity against most gram-positive bacteria, is administered intravenously once daily. It has a dual mechanism of action: It inhibits cell wall synthesis, like vancomycin, but also disrupts the function of the bacterial membrane, according to Theravance.

For approval, the company submitted the results of two double-blind, randomized phase III noninferiority studies of almost 1,800 adults with cSSSI caused by gram-positive bacteria, enrolled in 2005-2006. (Half of the 1,320 patients with microbiological confirmation of pathogens at baseline had MRSA.) The patients were treated with telavancin or vancomycin. The FDA and company analyses indicated that in both studies, treatment with telavancin for 7-14 days was as effective as with vancomycin—the current standard of care.

Adverse events with telavancin were mostly mild or moderate. The rate of renal adverse events among those on telavancin was 3.4%, compared with 1.2% among those on vancomycin; the rate of severe renal adverse events was also higher among those on telavancin (1.2% vs. 0.4%).

Cardiac-related severe adverse events were similar among those on telavancin and vancomycin (11% in both groups). Four patients on telavancin and six on vancomycin had a fatal cardiac event; two deaths in the telavancin group were possibly related to the drug, according to the FDA. ■