Newer, shorter-course antibiotic shows similar effectiveness for treating skin infection

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Treatment with a newer antibiotic, tedizolid phosphate, once daily for 6 days was statistically noninferior (no worse than) in efficacy to the antibiotic linezolid twice daily for 10 days for both early (at day 2 to 3) and sustained (at day 11) clinical responses in patients with acute bacterial skin and skin structure infections, according to a study appearing in the February 13 issue of *JAMA*.

"Antimicrobials available for treatment of complicated skin and skin structure infections (SSSIs) are generally efficacious, but antimicrobial resistance and adverse effects limit their use. Linezolid, an oxazolidinone [a class of antibiotics], is the only oral drug approved for complicated SSSI caused by methicillin-resistant *Staphylococcus aureus* (MRSA)," according to background information in the article. Sporadic outbreaks of linezolid-resistant strains of MRSA have been reported. Acute bacterial skin and skin structure infections (ABSSSIs) can be life-threatening and may require surgery and hospitalization. "Increasingly, ABSSSIs are associated with drug-resistant pathogens, and many antimicrobial agents have adverse effects restricting their use. Tedizolid phosphate is a novel oxazolidinone in development for the treatment of ABSSSIs."

Philippe Prokocimer, M.D., of Trius Therapeutics Inc., San Diego, and colleagues conducted a study to establish the noninferiority of tedizolid phosphate vs. linezolid in treating ABSSSIs and compare the safety of

the 2 agents. The phase 3, randomized trial was conducted from August 2010 through September 2011 at 81 study centers in North America, Latin America, and Europe. The intent-to-treat analysis set consisted of data from 667 adults ages 18 years or older with ABSSSIs treated with tedizolid phosphate (n = 332) or linezolid (n = 335). Patients were randomized to a 200 mg once daily dose of oral tedizolid phosphate for 6 days or 600 mg of oral linezolid every 12 hours for 10 days. The primary efficacy outcome was early clinical response at the 48- to 72-hour assessment (no increase in lesion surface area from baseline and oral temperature of 99.7°F or less, confirmed by a second temperature measurement within 24 hours). A 10 percent noninferiority margin was predefined.

The researchers found in the primary efficacy intent-to-treat (ITT) analysis, the response rates at the 48- to 72-hour assessment were 79.5 percent of 332 patients in the tedizolid phosphate group and 79.4 percent of 335 patients in the linezolid group. Sustained clinical treatment response rates at the end of treatment (day 11) were similar in the tedizolid phosphate and linezolid groups in the ITT analysis set (69.3 percent vs. 71.9 percent, respectively). Investigator-assessed clinical treatment response at the post-therapy evaluation (PTE) visit was also similar in the tedizolid phosphate and linezolid groups in the ITT analysis set (85.5 percent vs. 86.0 percent, respectively).

"Of particular interest are the similar treatment response rates in the tedizolid phosphate group (78.0 percent) and in the linezolid group (76.1 percent) in the sensitivity analysis that was based on the Foundation for the National Institutes of Health recommended outcome (≥ 20 percent decrease in lesion area)," the authors write.

Also, the researchers found that the clinical response rate at the PTE (7 to 14 days after completing therapy) was high (85 percent) for 178 patients infected with MRSA and similar in both the tedizolid phosphate

and linezolid treatment groups.

Treatment-emergent adverse events (mostly mild or moderate) occurred in 40.8 percent of patients in the tedizolid phosphate group and 43.3 percent of patients in the linezolid group. The overall incidence of serious adverse events was low and similar between groups.

"A short course of tedizolid phosphate was statistically noninferior to a 10-day course of linezolid for both early and sustained clinical responses in patients with ABSSSIs. Results were consistent for primary and sensitivity analyses, using either objective criteria or investigators' assessments, and treatment response rates were concordant for early and late time points," the authors conclude.

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