New antibiotic proven effective to treat acute bacterial skin infections

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A study published in today's *New England Journal of Medicine* reports that the antibiotic dalbavancin is as effective as vancomycin, the current standard-of-care antibiotic used to treat serious bacterial skin and skin-structure infections. The study results establish dalbavancin as a therapy for *Staphylococcus aureus* infections, including methicillin-resistant *S. aureus*, or MRSA. Acute bacterial skin and skin-structure infections are among the most common reasons for the hospitalization of adults in the United States today, and the associated medical costs are substantial.

A team led by Helen Boucher, M.D., Associate Professor of Medicine at Tufts Medical Center, reports the results in an article titled "Once-weekly Dalbavancin versus daily conventional therapy for skin infections ."

"Dalbavancin has a great likelihood of changing our practice in caring for patients with severe skin infections. It will now be possible to treat once a week instead of several times a day and will potentially remove the need for hospital admission and long-term intravenous catheters," Boucher said.

The team completed two clinical trials comparing efficacy of dalbavancin with vancomycin followed by linezolid. The Phase 3 studies, called non-inferiority trials, were conducted between 2011-2012. Titled DISCOVER 1 and DISCOVER 2 (Dalbavancin for Infections of the Skin COmpared to Vancomycin at an Early Response), the studies were conducted at 54 and 86 investigative sites, respectively, and were

randomized, double-blind, double-dummy trials. (To insure against bias, double-dummy trials include two placebo arms when the study drugs are administered by different methods, for example, orally versus intravenously.)

For the trial, the diagnosis of acute bacterial skin and skin-structure infection required the presence of cellulitis, a major abscess or a wound infection, all with at least 75 square centimeters of surrounding redness. Additional criteria were elevated body temperature and white blood cell count.

For a period of 10-14 days, patients were given either once-weekly intravenous dalbavancin or twice-daily intravenous vancomycin followed by oral linezolid, along with dummy infusions or pills. The primary endpoint was early clinical response, defined as cessation of spread of infection-related reddening and inflammation of the skin and the absence of fever at 48 to 72 hours. Secondary endpoints measured at the conclusion of therapy included clinical status and investigator's assessment of outcome.

Data from the two DISCOVER trials were pooled. Analysis showed that 525 of 659 (79.7 percent) in the dalbavancin group and 521 of 653 (79.8 percent) in the vancomycin-linezolid group had an early clinical response, indicative of treatment success. For patients infected with *Staphylococcus aureus*, including MRSA, clinical success was seen in 90.6 percent of the dalbavancin-treated patients and 93.8 percent of those treated with vancomycin-linezolid.

Dr. Boucher explained, "The patients in our study were very ill: more than 85 percent had fever at entry and more than half had systemic inflammatory response syndrome. In addition, our patients had large infections with median areas of over 300 square centimeters. Our results establish dalbavancin as an effective therapy and prove non-inferiority

of dalbavancin to vancomycin in the treatment of these serious infections."

In 2011, the Centers for Disease Control and Prevention identified antimicrobial resistance as a serious United States and global health concern. The DISCOVER trials were conducted with the help of the Generating Antibiotic Incentives Now (GAIN) provision of the 2012 Food and Drug Administration Safety and Innovation Act to stimulate development of new antibiotics to treat infections. Under the GAIN provisions, these drugs receive a priority review status and undergo an expedited regulatory approval process with FDA.

Provided by Tufts Medical Center