US hospitals testing experimental therapies to prevent two common bacterial infections

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The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, is supporting U.S. clinical sites participating in two ongoing international Phase 2 clinical trials evaluating investigational antibody-based therapies aimed at preventing potentially antibiotic-resistant infections. By aligning the NIAID Antibacterial Resistance Leadership Group (ARLG) with a large international consortium leading the effort, the U.S. investigators hope to enroll 30 adult patients from 15 intensive care units in the trials. NIAID is supporting the domestic sites with a grant to Duke University, Durham, North Carolina, which is part of the ARLG—a clinical research consortium working to reduce the impact of antimicrobial resistance. The larger international trials are supported by MedImmune, the global biologics research and development arm of AstraZeneca, based in Gaithersburg, Maryland, and the Brussels-based Innovative Medicines Initiative Joint Undertaking and the Combatting Antimicrobial Resistance in Europe (COMBACTE) consortium.

One trial, called EVADE, is evaluating the safety of the investigational medicine MEDI3902 (developed by MedImmune) and its ability to prevent pneumonia caused by *Pseudomonas aeruginosa*. The other trial, called SAATELLITE, is testing the safety of another investigational MedImmune medicine, suvratoxumab (previously known as MEDI4893), and its ability to prevent disease caused by *Staphylococcus aureus*. Both trials are randomized, placebo-controlled, and double-blind, meaning neither the participants nor the investigators will know who receives a placebo.

MEDI3902 and suvratoxumab are both monoclonal antibodies being investigated as preventive therapies. The medicines are not antibiotics but can be administered alongside standard antibiotic therapy. Monoclonal antibodies have been developed for use against diseases such as cancer, Ebola and respiratory syncytial virus, but rarely have been used to target bacterial pathogens.

The World Health Organization recently included *P. aeruginosa* and *S. aureus* on a list of antibiotic-resistant bacteria that pose the greatest risk to human health. People in healthcare settings with weakened immune systems, especially those on breathing machines or with catheters, face an increased risk of becoming seriously ill from these infections.

According to the Centers for Disease Control and Prevention, Staphylococcus bacteria are a leading cause of healthcare-associated infections, such as pneumonia, bacteremia, and heart valve and bone infections. In 2011, methicillin-resistant *S. aureus* (MRSA) caused more than 80,000 serious infections and 11,285 related deaths in the United States, according to the CDC. *P. aeruginosa* can cause bloodstream infections and pneumonia that can be fatal. Approximately 51,000 healthcare-associated *P. aeruginosa* infections occur each year in the United States, and about 6,700 of these are drug-resistant, leading to more than 400 deaths annually, according to CDC estimates based on a 2011 survey.

"It is becoming increasingly common for hospitalized patients—especially those with weakened immune systems—to develop severe, hard-to-treat bacterial infections," said NIAID Director Anthony S. Fauci, M.D. "These clinical trials testing monoclonal antibodies as novel preventive therapies are part of a global collaborative effort to explore innovative ways to mitigate the threat of antimicrobial resistance."

All participants in both the EVADE and SAATELLITE trials will be on mechanical ventilation in the intensive care unit at the time of enrollment. Trial investigators will provide information about the purpose and possible risks and benefits of the study so that patients can ask questions before they agree to participate. If a patient is unconscious or otherwise unable to consent during the screening process, a legally authorized representative can provide initial consent.

Participants in the EVADE trial must be colonized with *P. aeruginosa* bacteria in the lower respiratory tract but display no signs of pneumonia. They will be randomly assigned to receive either one intravenous (IV) infusion of MEDI3902 or placebo. Investigators will check for incident pneumonia caused by *P. aeruginosa* for 21 days, and will monitor participants for 49 days total.

Similarly, participants in the SAATELLITE trial must be colonized with *S. aureus* in the lower respiratory tract but free of *S. aureus*-related disease. They will be randomly assigned to receive either one IV infusion of suvratoxumab or a placebo. Investigators will evaluate the incidence of *S. aureus*-related pneumonia for 30 days, and monitor participants for 190 days total. Participants in both the EVADE and SAATELLITE trials will be regularly evaluated for any treatment-related safety issues.

Thomas Holland, M.D., of Duke University is the coordinating physician for the U.S. sites. Jean Chastre, M.D., of Groupe Hospitalier Pitie-Salpetriere in Paris serves as overall principal investigator for the EVADE trial, and Bruno Francis, M.D., of Centre Hospitalier Universaitaire de Limoges in Limoges, France serves as overall principal investigator for the SAATELLITE trial.

For more information about the trials, visit ClinicalTrials.gov and search identifiers NCT02696902 and NCT02296320.