Trial of investigational Ebola treatments begins in Democratic Republic of the Congo

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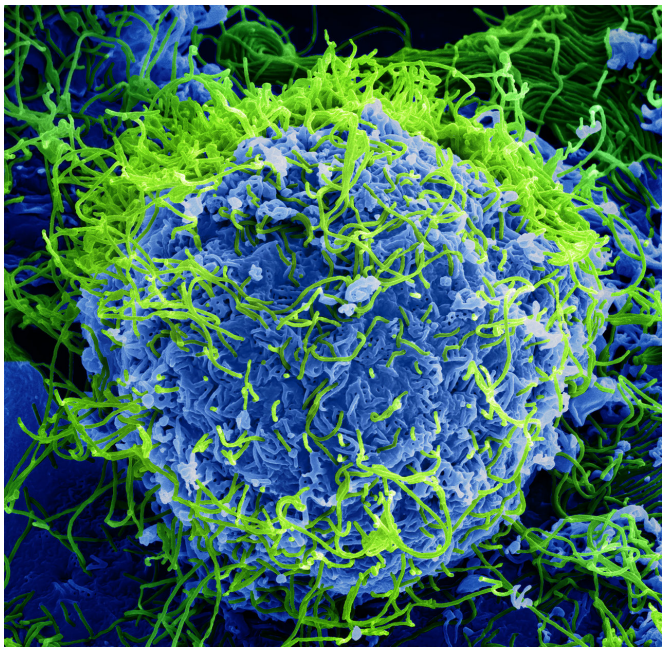

Colorized scanning electron micrograph of Ebola virus particles (green) both budding and attached to the surface of infected VERO E6 cells (blue). Image captured and color-enhanced at the NIAID Integrated Research Facility in Fort Detrick, Maryland. Credit: NIAID

An international research team has begun patient enrollment in a clinical trial testing multiple investigational Ebola therapies in the Democratic Republic of the Congo (DRC). The randomized, controlled trial is enrolling patients of any age with confirmed Ebola virus disease (EVD) at a treatment unit in the city of Beni operated by The Alliance for International Medical Action (ALIMA), a medical humanitarian organization.

The trial, which will expand to additional DRC districts, is organized through an international research consortium coordinated by the World Health Organization (WHO). It is led and funded by the National Institute for Biomedical Research (INRB), part of the DRC Ministry of Health, and the National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. National Institutes of Health, and also involves several additional international partners.

"Combatting Ebola requires a comprehensive response that draws on the strengths of all areas of public health. Biomedical research can lead to critical new tools, such as potentially life-saving therapies," said NIAID Director Anthony S. Fauci., M.D. "Through scientifically and ethically sound clinical trials, we hope to efficiently and definitively establish the safety and efficacy of these investigational Ebola treatments, offering new ways to save lives."

On August 1, 2018, the DRC Ministry of Health declared the country's 10th outbreak of EVD. As of November 25, 2018, 240 deaths out of 419 confirmed and probable cases of EVD have been reported in the northeastern provinces of North Kivu and Ituri. Under the leadership of the DRC Ministry of Health, the WHO has coordinated the outbreak response with several international partners. NIAID, along with the U.S. Centers for Disease Control and Prevention, the U.S. Agency for International Development (USAID), and other U.S. government partners, have provided guidance and support to the multi-sectoral outbreak response.

"We urgently need a safe and effective treatment for this deadly disease," said DRC Minister of Health Oly Ilunga Kalenga, M.D., Ph.D. "As we face a 10th outbreak of Ebola, we hope this clinical trial will give us more information about how best to treat patients."

The trial aims to compare mortality among patients who receive one of three investigational Ebola drugs with a control group of patients who receive the investigational monoclonal antibody cocktail treatment ZMapp, developed by Mapp

Biopharmaceutical, Inc. The therapies being tested include: mAb114, a single monoclonal antibody developed by NIAID, with early support from the INRB; and remdesivir (also known as GS-5734), an antiviral drug developed by Gilead Sciences, Inc. The trial has been approved to begin enrolling patients in these three groups, and plans are underway to amend the trial to include REGN-EB3 (also known as REGN3470-3471-3479), a monoclonal antibody cocktail developed by Regeneron Pharmaceuticals, Inc.

The participating Ebola treatment units will continue to provide all participants with supportive care for EVD. Ebola care includes supportive oral and/or intravenous fluids, electrolyte replacement, maintaining oxygen status and blood pressure, and pain management.

The investigational treatments have varying levels of data to support their use from testing in the laboratory, animals, and humans. However, none has been approved for treating EVD. ZMapp is the only investigational treatment previously tested in a randomized, controlled efficacy trial. Results from that study, conducted in the U.S. and West Africa during the 2014 to 2016 outbreak, suggested that ZMapp appeared to be beneficial, but as the outbreak waned, the trial ultimately could not enroll enough participants to definitively establish the drug's efficacy.

The investigational treatments also have been administered to most of the Ebola patients in the current outbreak in the DRC under an ethical framework developed by the WHO called Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI). However, this emergency-use mechanism cannot yield generalizable evidence on how well the treatments work.

"A randomized, controlled clinical trial is necessary to obtain reliable data about the safety and efficacy of investigational Ebola treatments," said H. Clifford Lane, M.D., director of NIAID's Division of Clinical Research. "It is possible to conduct rigorous clinical research in an outbreak setting, and we anticipate this trial will provide useful data."

Professor Jean-Jacques Muyembe-Tamfum, M.D., Ph.D., director-general of the INRB, and Richard T. Davey, Jr., M.D., deputy director of NIAID's Division of Clinical Research, are co-principal investigators for the study.

Trial participants will be randomly assigned to receive one of the investigational treatments by intravenous infusion. Site clinicians will monitor patients' symptoms and take blood samples for laboratory tests. Patients will remain in the Ebola treatment unit until they fully recover from the disease. They will be asked to return to the clinic approximately two months after receiving treatment for a check-up and to provide additional blood samples for laboratory tests.

Plans are underway to expand the trial beyond the ALIMA site in Beni to additional Ebola treatment units operated by medical humanitarian organizations, including International Medical Corps. The trial also may be adapted to continue across more than one outbreak and in several countries. The number of participants enrolled in the trial ultimately will depend on the evolution of Ebola outbreaks. The study is designed to enroll 112 patients per arm, potentially over multiple outbreaks.

"This clinical trial marks a significant and important step forward for the DRC and our international partners," said Dr. Muyembe. "We are eager to learn more about each of these investigational treatments as we continue to work tirelessly to identify new cases, trace contacts and control the spread of disease."

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