Ebola: Promising Early-Stage Safety Clinical Trial Results For Potential Treatment Based On Antibodies Isolated In Switzerland

A Phase 1 clinical trial to test the safety of an antibody to use against Ebola outbreak has been successfully concluded by the National Institutes of Health (NIH) Clinical Center in Bethesda, Maryland (U.S.A.). The treatment is based on the monoclonal antibody mAb114, which was isolated and characterized in Switzerland at the Institute for Research in Biomedicine (IRB Bellinzona, affiliated to USI Università della Svizzera italiana) in collaboration with Humabs BioMed SA, a subsidiary of Vir Biotechnology Inc., San Francisco, and with scientists at the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC); National Institute of Biomedical Research (INRB) in the DRC; and the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick, Maryland. The results published in *The Lancet* reveal that mAb114 appears to be safe, well tolerated, and easy to administer.

Clinical Phase 1 design

In the Phase 1 study, that began in May 2018, aimed at testing whether mAb114 is safe and how a person's body responds to it. Participants received a single intravenous infusion of mAb114, administered over approximately 30 minutes. Participants were divided into three groups that received different dosages. The National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC), part of NIH, developed the investigational treatment and conducted and sponsored the clinical trial.

Phase 1 results

All infusions were well tolerated. Four participants reported mild side effects, such as discomfort, muscle or joint pain, headache, nausea, and chills in the three days following the infusion. As expected, levels of mAb114 in the blood increased as the dosage was increased. Investigators also observed relatively uniform levels of absorption, distribution, and elimination of mAb114 among participants.

Experimental Ebola treatments used for the first time against an active outbreak in Congo

The Ebola virus causes hemorrhagic fever with a mortality rate of up to 90% and periodically triggers outbreaks in several African countries, as it is the case since mid-2018 in the Democratic Republic of the Congo (DRC). There is currently no approved Ebola therapy or vaccination. However, it is known that Ebola infection survivors carry life-long immunity preventing further infections.
In the light of the Phase 1 positive clinical trial results, the investigational treatment is currently being offered to Ebola patients in the DRC under compassionate use and as part of a Phase 2/3 clinical trial of multiple investigational treatments.
It is the first time that the antibody mAb114 against the Ebola virus is being tested against an active outbreak of the deadly virus with patients in Congo.

Potential Advantages of mAb114

The authors of The Lancet paper note several potential advantages for deploying mAb114 in an outbreak setting, including the ease and speed of its administration, and its formulation as a

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freeze-dried powder that does not require freezer storage. The powder is reconstituted with sterile water and added to saline for administration.

mAb114 isolation and characterization
The collaboration between scientists at the IRB, Humabs BioMed SA, the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC), the National Institute of Biomedical Research (INRB) in the DRC; and the U.S. Army Medical Research Institute of Infectious Diseases at Fort Detrick, Maryland, have led to the isolation – from blood of a survivor of the 1995 Ebola outbreak – of two lead human antibodies (code-named mAb100 and mAb114) against Ebola (more info) and its characterization. The most promising one, mAb114, has been manufactured and developed for clinical testing with the support of the Defense Advanced Research Projects Agency (DARPA, Arlington, USA).

Comments

"This is an important step forward in the fight against this lethal virus. It comes from a joint effort from five different institutions and illustrates the power of the human antibody technology developed at IRB and Humabs" said Antonio Lanzavecchia, MD, Director of the IRB and Principal Investigator of this study at the IRB.

"The isolation of this human antibody is another validation of our approach that can potentially lead to effective treatments against deadly infectious diseases," said SVP Antibody Research Davide Corti, PhD. "It is one of our main objectives and source of motivation to have our antibodies used in the Phase 2/3 trial to potentially treat patients, and hopefully save lives" added Filippo Riva, Managing Director of Humabs BioMed.

ARTICLE:
MR Gaudinski et al. Safety, tolerability, pharmacokinetics, and immunogenicity of the therapeutic monoclonal antibody mAb114 targeting Ebola virus glycoprotein (VRC 608): an open-label phase 1 study. *The Lancet* DOI: 10.1016/S0140-6736(19)30036-4 (2019).

About the National Institutes of Health (NIH): NIH, the U.S.'s medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

About the IRB: Founded in 2000 in Bellinzona, it is affiliated with the USI Università della Svizzera italiana since 2010. Funded by private and public institutions and competitive financing, the IRB hosts 13 research groups and 120 researchers working on studying different defense mechanisms in the body to fight infections, tumors and degenerative diseases. With more than 600 publications in main scientific journals, the IRB has gained international recognition as a center of excellence for immunology and cell biology. In particular, Lanzavecchia's laboratory investigates the mechanisms of antibody-mediated resistance to infectious diseases. They use high-throughput cellular screens to isolate potent and broadly neutralizing antibodies, which can be developed for prophylaxis and treatment of infectious diseases and used as tools for vaccine design. www.irb.usi.ch

About the Humabs BioMed SA, a subsidiary of Vir Biotechnology, Inc., San Francisco, California: Based in Switzerland, it is focused on discovering and developing fully human monoclonal antibodies to treat serious infections. Humabs BioMed was incubated in the Institute for Research in Biomedicine (IRB). Humabs' proprietary discovery technology - CellClone - platforms enable the isolation of antibodies that have passed natural selection by the human immune system in response to disease and can generally be developed rapidly without extensive lead optimization. Humabs was acquired by Vir Biotechnology, Inc., in 2017. Vir integrates diverse innovations in science, technology, and medicine to potentially transform the care of people with serious infectious diseases. Vir is taking a multi-program, multi-platform approach to applying these breakthroughs, including the development of possible treatments that induce protective and therapeutic immune responses. Vir's scale and scope, together with leading scientific and management expertise, allow it to perform significant internal R&D, in-license or acquire innovative technology platforms and assets, and fund targeted academic research. The company is headquartered in San Francisco, California, with operations in Portland, Oregon, Boston, Massachusetts, and Bellinzona, Switzerland.
www.vir.bio , www.twitter.com/vir_biotech

Photo caption:

May 21, 2018 – A healthy volunteer receives an intravenous infusion of mAb114—an experimental treatment for Ebola virus disease—in a Phase 1 clinical trial held at the NIH Clinical Center in Bethesda, Maryland. Credit: NIAID

Contact:
Humabs BioMed SA
+41 91 825 63 80