The Liberia-US Joint Clinical Research Partnership

The Partnership

What is the Liberia-US Joint Clinical Research Partnership?
The Liberia-US Joint Clinical Research Partnership is a collaboration between the Government of Liberia and the Government of the United States (USG). The partnership will study common infectious diseases in Liberia and is developing Liberian clinical research capacity.

How did the Liberia-US Joint Clinical Research Partnership start?
In August 2014 the Liberian Minister of Health and Social Welfare (MOHSW), Minister Walter Gwenigale, wrote a letter to the U.S. Secretary of Health and Services, Sylvia Burwell, to ask for a Liberia-US collaboration to conduct clinical research to develop vaccines and treatments for Ebola. Secretary Burwell accepted and asked the National Institutes of Health (NIH), specifically the National Institute of Allergy and Infectious Diseases (NIAID), to be part of the partnership for the US.

What organizations are involved in the Government-to-Government partnership?
Both governments are drawing on scientists and clinical researchers to advance the research on Ebola. The Liberian MOHSW has drawn on expertise from University of Liberia, the Liberian Institute for Biomedical Research, and the Post Graduate Liberian Medical Education Program to form the Liberian team. Additional substantive contributions in Liberia have come from the Liberian Medicines and Health Products Regulatory Authority (LMHRA), the National Research Ethics Board (NREB), and the Incident Management System (IMS). The USG has called on scientists from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, to form the USG team. The US Centers for Disease Control and Prevention (CDC), the US Food and Drug Administration (FDA), the Biomedical Advanced Research and Development Authority (BARDA), the US Department of Defense (DOD), the United States Agency for International Development (USAID), and other USG agencies are helping as well. The Liberian traditional and community leaders are providing valuable advice on the program too.

The Ebola Vaccine Study

Why is the Ebola vaccine study the first study? Why is the study being done in Liberia?
The World Health Organization (WHO) put out a call for fast-tracking research to develop an Ebola vaccine. Liberia is one of the three countries in West Africa hardest hit by the recent Ebola epidemic. Currently no vaccines are available to prevent people from getting Ebola. It is hoped that this vaccine study will contribute to the development of effective vaccines to protect people in Liberia and elsewhere from Ebola. Vaccines have to be tested first to see whether they are safe in people and whether they can prevent disease. Some common approved vaccines that have gone through such testing are those for polio, measles, and tetanus.

What are the vaccines being tested in this study?
There are two Ebola vaccines being studied. One, manufactured by GlaxoSmithKline (GSK), is called the cAd3EBO-Z vaccine. The second is a vaccine called rVSV-ZEBOV, which is manufactured by NewLink/Merck. Both contain a small genetic piece of the Ebola virus carried into the body by another harmless virus. This small piece of Ebola triggers an immune response to outer coat of the Ebola virus, meaning it teaches the body how to fight off Ebola if it meets the virus. It is anticipated that this immune response will prevent people who receive the vaccine from getting Ebola.

What is the design of this study?
The study is called a double-blind randomized placebo-controlled Phase 2/3 trial. This means that the people in the study are picked by chance, or lottery, to receive either one of the experimental

preventing Ebola vaccines or a simple saltwater injection. "Double-blind" means that neither the study doctors nor the people in the study know which of the vaccines or the placebo anybody gets. Phase 2/3 means the study will look at the safety of the vaccine and figure out if either of the vaccines will prevent Ebola.

Who will be enrolled into the vaccine study?
People can join the study if they are 18 year or older, plan to be in Monrovia for at least a year, and have a normal temperature.

Can someone get Ebola from the study vaccines?
No. It is not possible to get Ebola from the vaccines being studied because they do not contain the whole Ebola virus. Only the whole Ebola virus can cause an infection. The vaccines contain only a small piece of the Ebola virus envelope that helps the body learn how to fight Ebola.

What happens if a study vaccine does work?
If one of the study vaccines is found to work the study will be stopped as soon as possible and all participants will be given the effective vaccine, if they want it.

What should a study participant do if he or she develops possible symptoms of Ebola?
Study participants will be given the information about who to call if they feel sick. If they think they may have Ebola, they should contact their study team quick-quick.

The Ebola Treatment Study

What studies will be done to test treatments for people with Ebola?
The Liberia-US collaboration will test treatments to see if they can help people with Ebola survive. The treatment study will compare promising medicines to the current standard of care. The first treatment to be studied will be ZMapp. The treatment study will start sometime after the vaccine study starts.

What is ZMapp? How does it work?
ZMapp is a mixture of three antibodies that attach to the Ebola virus and help reduce the amount of virus in the body. Studies have shown that reducing the amount of Ebola virus can help people survive.

How is ZMapp given?
ZMapp will be given with a drip using a tiny needle into the vein.

How will the study team know if the ZMapp works?
Participants in the study will randomly be assigned to one of two groups, the ZMapp group or the normal care group. The study team will compare the two groups for survival and time to getting better.

Who can participate in the ZMapp study?
People with Ebola who go to an Ebola Treatment Unit that is participating in the treatment study can learn about the study and choose to participate.

Which Ebola Treatment Units (ETUs) are participating in the study?
Several ETUs will be participating in the study. The Monrovia Medical Unit and the ELWA ETU will participate in the study.

Liberia-United States Joint Clinical Research Partnership Announces Start of Large Clinical Study of Vaccines to Prevent Ebola

Monrovia, Liberia - February 2, 2015

The Liberia-U.S. Joint Partnership for Clinical Research announced that a clinical study of two experimental vaccines to protect against Ebola begins in Liberia today. The Partnership for Research on Ebola Vaccines in Liberia (PREVAIL) study is designed to determine if giving a single dose of a test vaccine will prevent Ebola virus disease (EVD). The two vaccines to be tested in this study are the ChAd3-ZEBOV vaccine, manufactured by Glaxo SmithKline, and the rVSV-ZEBOV vaccine, manufactured by Merck/NewLink.

The PREVAIL study originated with a request last August from the Liberian Minister of Health to the U.S. Secretary of the Department of Health and Human Services to form a joint clinical research partnership to accelerate the development of vaccines to prevent Ebola and medicines to treat people with EVD. When this collaboration began in October 2014, EVD was ravaging Guinea, Liberia, and Sierra Leone. The uncontrolled outbreak prompted a World Health Organization (WHO) panel of experts to advise the global scientific community to accelerate the development of Ebola vaccines and treatments without compromising international standards for safety and efficacy. The two vaccines selected for this study were recognized by the WHO panel as being at the most advanced stage of development.

"This initiative represents an important entry into the global clinical research arena for Liberia and an enduring symbol of the strong ties that exist between Liberia and the United States," said Fatorma Bolay, PhD, Liberia Co-Principal Investigator for the study. "Most importantly, it shows the invaluable significance of a combined global effort to find safe and effective vaccines to control the spread of this devastating disease and prepare the world to prevent future epidemics," he added.

The PREVAIL study protocol has been diligently reviewed for scientific rigor and ethics, and has been approved by the U.S. Food and Drug Administration (FDA), an Institutional Review Board of the U.S. National Institutes of Health, the National Research Ethics Board of Liberia, and the Liberia Medicines and Health Products Regulatory Authority.

Approximately 27,000 healthy adult volunteers are expected to participate in the PREVAIL study at 10 or more clinical centers in and around Monrovia, Liberia. Study participants will be assigned at random, or by chance, into one of three groups to receive either the ChAd3-ZEBOV vaccine, the rVSV-ZEBOV vaccine, or a saline (saltwater) injection, known as a placebo. Each group will have about 9,000 people. Neither the volunteer nor the study staff will know which vaccine or placebo has been administered until the end of the study. All participants will be given advice on how to avoid being infected with Ebola.

This type of study design, called a randomized controlled study, compares the results from the volunteers who receive the experimental vaccines against the results from those who receive the

placebo (control). If one or both of the test vaccines are safe and effective, it is expected that those volunteers who received those vaccines will be protected from EVD.

In developing the study, the study sponsor, the U.S. National Institutes of Health, thoroughly considered concerns expressed about the ethics of exposing a subset of otherwise healthy people participating in the trial to a placebo control that offers no protection against EVD. The randomized placebo-controlled design is considered the most powerful for determining if a test vaccine or treatment is effective, however, and the use of a placebo is considered scientifically appropriate and ethical when no other approved medical alternative exists. The PREVAIL study will ensure that study participants receive the optimum standard of care available in the country should they either become infected with the Ebola virus or develop any unexpected or dangerous reactions to the vaccine (adverse events).

The first 600 vaccinations will occur at the newly renovated clinical research unit of the Redemption Hospital in New Kru Town. Volunteers will be given a detailed explanation of the purpose of the study, what procedures the study entails (e.g., collection of urine and blood samples), the side effects or discomforts that could occur after receiving the vaccination, and any possible benefit that could come from their participation. Each volunteer will be given the opportunity to have their questions answered before making their own decision about whether or not to participate. This informed consent process, which has been thoroughly reviewed by research ethics boards in Liberia and the U.S., will occur with every potential participant. Those who join the study must first sign an informed consent form before any study procedure or vaccination is performed. Potential volunteers will be advised that they are at liberty to decline participation or withdraw their consent at any time without consequence.

All participants will be closely monitored by the study staff. An independent Data and Safety Monitoring Board of medical and scientific experts from the U.S. and Liberia will also periodically review data collected from study participants to ensure their safety.

The clinical development process for the test vaccines began with Phase 1 testing for safety (assessment of side effects or adverse events) in a small number of human volunteers. Several Phase 1 studies of Chad3-ZEBOV and rVSV-ZEBOV have been conducted and most of the adverse events reported in these studies were mild and did not last long. A few study volunteers experienced fever and joint pain that lasted for a few days and ended within two weeks. T Most people who received the vaccines in these studies developed infection-fighting proteins, or antibodies, that might help to protect them from getting EVD.

The Liberia-U.S. Clinical Research Partnership team has worked diligently over the past three months with leaders and members of various Liberian communities to ensure that the initiation and conduct of the PREVAIL study are locally and nationally appropriate. In addition to Dr. Bolay, the study is being led by Stephen B. Kennedy, MD, MPH, FLCP, Liberia Co-Principal Investigator, and from the United States H. Clifford Lane, M.D., Clinical Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health.

Frequently Asked Questions about Ebola Vaccines

How did the Ebola vaccine study come about?
The World Health Organization (WHO) put out a call to speed up the process of making an Ebola vaccine. The Governments of Liberia and the United States formed a partnership to answer the call. The goal of the partnership is to learn more about Ebola. They want to find a vaccine to prevent Ebola. They also want to find treatments that can heal people who are sick with Ebola.

Who is paying for this vaccine study?
The Liberian Ministry of Health and Social Welfare and the US National Institutes of Health are both supporting and financing the Ebola vaccine study.

Will the vaccines work?
We do not know if the vaccines will prevent Ebola. That is the purpose of the study.

Why is this study being done in Liberia?
Liberia is one of the three countries in West Africa hardest hit by the recent Ebola epidemic. It is expected that the vaccine study will contribute to the development of effective vaccines to protect people in Liberia and elsewhere from Ebola.

What vaccines are being tested in the study? Who makes them?
There are two test Ebola vaccines and one saltwater injection, or placebo. One vaccine was developed by the US National Institutes of Health (NIH) and now GlaxoSmithKline has the contract to make this vaccine. The other vaccine was developed by the Public Health Agency of Canada (PHAC) and now the companies New Link and Merck have the contract to make the second one.

How are the vaccines supposed to work?
Each vaccine has a small piece of the Ebola virus in it. It is too small to make a person sick with Ebola but enough to teach the body how to fight the virus. This means that the body makes an immune response to Ebola. So if the body sees Ebola again, it knows how to fight it well. It is expected that this immune response will protect people from Ebola.

What is the reason for testing two vaccines?
It is not known whether either of the vaccines will prevent Ebola. The two test vaccines are different in how they are made to work. Both vaccines prevent Ebola in animals. In smaller safety studies in humans that have already been done in Africa, Europe, and the US, the vaccines appear safe. This study will try to find out if one or both of the test vaccines prevent Ebola in people. This study will also make sure that the vaccines are safe in large numbers of people.

Who can join the study?
People can join the study if they are 18 years or older, plan to be in Monrovia for at least a year, and have a normal temperature.

How many people can join the study?
The study will include about 27,000 people. There will be three groups with about 9,000 people in each group. Two groups will receive one of the two test vaccines and one group will receive the saltwater injection.

Which groups of people are most wanted for this vaccine study?
People at high risk for Ebola are most wanted for the study. These groups include people in communities where there is Ebola now, people who live near or with people who have Ebola, burial teams, health care workers, spouses of Ebola survivors, ambulance workers.

Will the study volunteers choose which vaccine they want?
No. Study volunteers will be chosen at random to receive either one of the two vaccines or to a harmless injection of saltwater. The study participant and the study staff will not know which group the participant is in until the end of the study.

Do the test Ebola vaccines have side effects?
The test Ebola vaccines can cause side effects in some people. Some people who receive the vaccine have pain, redness, or swelling in the arm of the injection. Other side effects include 1 to 2 days of fever, headaches, mouth sores, fatigue, and not feeling hungry. Some people have joint pain for a few weeks.

What happens if someone gets sick due to the vaccine?
If a person in the study gets sick from the vaccine, he or she should contact the study staff by calling the number on the card given out at the time of joining the study. The study staff will help arrange care for this person. Study staff will decide whether the illness may have been caused by the vaccine. This person will receive care at the clinics and hospitals free of charge.

Who is responsible to care for those with side effects?
The study team will arrange care for participants with side effects. The care will be free.

Can someone get Ebola from the study vaccines?
No. It is not possible to get Ebola from the vaccines being studied because the vaccines do not contain the whole Ebola virus. Only the whole Ebola virus can cause Ebola. The vaccines contain only a small part of the Ebola virus to help trigger an immune response against the virus.

Why can't children participate in the vaccine study? They would benefit from an Ebola vaccine.
We do not know if the vaccine is safe for children. Studies are being planned in other countries to test the safety and immune responses in children.

How will people be cared for if they are injured?
If there are vaccine-related side effects, people will receive free care arranged by the study team.

Will the people in the study be paid?
People in the study will be given money to cover their transportation and missed work. This is called compensation for inconvenience.

What is ZMapp?
ZMapp is a possible treatment for people who have Ebola virus disease. ZMapp is not a vaccine. It is a mix of three infection-fighting antibodies. We do not know if ZMapp will help people with Ebola virus disease get better. The Ebola vaccine study will not include ZMapp. A different study planned for Liberia will see if ZMapp can help people sick with Ebola get better.

Why will the vaccine study start at Redemption Hospital?
Redemption Hospital is close to communities that have suffered from Ebola. The leaders of Redemption welcomed the study team to start the study at Redemption. Other sites will be added after the first 600 people join the study.

What is the benefit of participating?
There may not be any benefit from participation in the vaccine study. If the study learns that one of the vaccines works to prevent Ebola and is safe, all the study participants will receive the vaccine at the end of the study.

If I participate in the vaccine study can I expose myself to Ebola?
No. We do not know if the vaccines in the study will work to prevent Ebola. If you participate in the study, you must continue to protect yourself from Ebola.

Contact List

For more information or to schedule an interview regarding the vaccine study, please contact:

Liberian Co-investigators:

Stephen B. Kennedy, MD, MPH, FLCP
+231-886-645830
kennedys@lpgmc.org

Fatorma Bolay, PhD
+231-886-513040
director.libr@gmail.com

US Principal Investigator:

H. Clifford Lane, MD
Inquiries to doepel@nih.gov or niaidnews@niaid.nih.gov or
NIAID Office of Communications at +1-301-402-1663