INSTITUTE: National Institute of Allergy and Infectious Diseases

STUDY NUMBER: 17-I-0059 PRINCIPAL INVESTIGATOR: Matthew J. Memoli MD, MS

STUDY TITLE: Randomized, Double-Blind, Placebo-Controlled, Phase 1 Study in Healthy Volunteers to Evaluate the Safety and Immunogenicity of AGS-v, a Universal Mosquito-Borne Disease Vaccine

Continuing Review Approved by the IRB on 01/22/18
Amendment Approved by the IRB on 04/02/18 (D) Date Posted to Web: 04/05/18
Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

PURPOSE OF THE STUDY

Mosquito-borne diseases continue to cause significant health problems and death worldwide despite on-going control efforts. Mosquitos transmit viruses like dengue, yellow fever, West Nile virus, chikungunya, Rift Valley fever, Japanese encephalitis, and Zika virus. These viruses can spread quickly and can be difficult to control.

SEEK, a London-based pharmaceutical company, has developed the AGS-v vaccine that targets proteins in the mosquito saliva. By doing so, it may help prevent multiple mosquito-borne diseases and possibly reduce the lifespan of a mosquito that bites a vaccinated person. This is an experimental vaccine and we need to study it further to see if it is safe in humans. We also need to see how it affects the human immune system. This is the first time this vaccine will be used in

humans. It has been approved by the US Food and Drug Administration (FDA) for use in this study only. It has not been approved for public use.

The vaccine is made entirely of man made protein-based products that are the same as ones found in mosquito saliva. The vaccine does not contain actual mosquito saliva. The vaccine does not come from any virus or other infectious material. You cannot get a mosquito-borne illness from this vaccine. All of the vaccine components were manufactured in a laboratory or factory. The purpose of this study is to see if the vaccine is safe. We also want to see if it activates your immune system against mosquito saliva. We do not know, and we won't be able to tell from this study, if the vaccine will protect you from mosquito-borne illnesses.

Your participation in this study will be about 1 year.

CRITERIA TO TAKE PART IN THIS STUDY

You are being asked to participate in this study because you are a healthy adult who meets the age requirement and has completed the screening process. You may participate if you:

- meet all of the study requirements,
- are willing to have your samples stored for future research,
- agree to not drink alcohol for 24 hours prior to each study visit,
- agree to not donate blood or blood products throughout the study, and
- agree to all of the study procedures described below.

If you are female, you cannot be breast-feeding or pregnant. Additionally, you cannot become pregnant during this study. This means you must be postmenopausal, surgically sterile, abstain from reproductive sex, or use contraceptives. Adequate contraception is considered the use of condoms with spermicide plus one additional form of birth control such as an intrauterine device, a diaphragm, or contraception that is oral, injected, or implanted. Both men and women need to use contraceptives for 4 weeks prior to study start, and continue to use them for 12 weeks after the second vaccine.

Participation in this study is entirely voluntary. Declining to participate in this study will in no way affect your relationship with the NIH or the NIH staff.

STUDY PROCEDURES

The study will take place in the Clinical Center (CC) on the NIH campus in Bethesda, MD. The following procedures and tests will be administered intermittently throughout the study. A member of the study staff will explain the schedule and let you know how often each procedure will be performed.

Day 0	Medical history, exam and vaccination
Day 7 (± 2 days)	Follow-up visit with symptom diary
Day 14 (± 2 days)	Follow-up visit
Day 21 (± 2 days)	Vaccination
Day 28 (± 2 days)	Follow-up visit with symptom diary
Day 35 (± 2 days)	Follow-up visit

Day 42 (+ 14 days)	Mosquito feeding
Day 44 (or +2 days after mosquito feeding)	Phone call follow up
Follow up visits every ~60 days (± 14 days) X5	

Medical History: The study team will review your medical history with you, including medications you are taking now and have taken recently.

Physical Exam: The study team will perform a complete physical examination including blood pressure, heart rate, respiratory rate, temperature, height, weight, and finger-measured oxygen level.

Vaccination: You will be randomly assigned (in a manner similar to picking a number out of a hat) to receive the vaccine with adjuvant, the vaccine without adjuvant, or the placebo. The adjuvant is a booster for the vaccine's effect on your immune system. The placebo is a saline solution that has no measurable effect on the body. You and your doctors will not know if you have been given the vaccine with or without adjuvant or the placebo. The pharmacy staff will know which drug you are taking. You will then receive the vaccine or placebo via injection with a needle and syringe in the fatty tissue of your arm near the shoulder. A nurse trained by study staff will administer the vaccine or placebo. We will watch you for 2 hours after the injection and monitor your vital signs.

Symptom Diary: For 7 days after each vaccination (Days 0-7 and 21-28) we will need you to record some information. You will be given a booklet to record this information. This includes: temperature, any symptoms you have, and any redness at the site of vaccine. You will also need to document if you have any mosquito bites, and if possible, take pictures of them. We will give you with a thermometer to take your temperature. We will give you a ruler to measure any redness on your arm. You will need to bring the booklet with you to each visit.

Blood Draws: A blood draw involves using a needle or syringe to remove blood from your vein. The amount of blood drawn during the study is approximately 3 cups of blood over the entire length of the study, including the follow-up period. This amount is within the limits allowed by the NIH Clinical Center for research purposes. For comparison, if you were to donate blood, the amount of blood that is taken at one time is approximately 2 cups.

Urine Collection: We will collect your urine for routine laboratory testing and illegal drug testing.

Mosquito Feeding: Three to five weeks after you receive the second vaccine, you will undergo a mosquito feeding. This is done with mosquitos grown in the insectary at the NIH. These mosquitoes have been grown in a controlled environment in isolation to prevent them from contracting or carrying any human diseases. First, an intravenous catheter will be placed in your arm to facilitate blood draws. Then, around 5 to 10 *Aedes aegypti* mosquitos will be allowed to bite your arm via a feeding device for 20 minutes. These mosquitos have no viruses or parasites, so they cannot give you a mosquito-borne disease. Your blood will be collected prior to the feeding and then 30, 60, 120, and 180 minutes after the mosquitos have fed on your arm.

Phone Call: A member of the study team will call you two days after your mosquito feeding to see how you are doing and if there is any redness or discomfort remaining from the mosquito bites on your arm.

RISKS

Risks from the study vaccine

The vaccine used in this study is investigational and has not been studied in humans. Therefore, we do not know precisely what side effects may occur in humans. However, animal studies in mice and rabbits have shown the vaccine to be well-tolerated and non-toxic. Furthermore, the SEEK company that makes this vaccine has used the same technology to make other vaccines. In these studies, people only had minor vaccine reactions, and no severe vaccine reactions have been observed in any participants receiving these vaccines. The adjuvant, or "booster" part of the vaccine, can cause more severe inflammation or irritation in the fatty layer of the skin, but this is a rare event and has not been seen in SEEK's other vaccine studies with this adjuvant. The adjuvant has the potential to cause autoimmune disease, but this has not been observed and would be unexpected.

Vaccine reactions must be considered a risk of all vaccines. A minor vaccine reaction typically occurs within a few hours of injection and resolves within a short period of time posing little risk to the participant. Symptoms include local pain, swelling, and redness at the site of injection and may include systemic symptoms like fever, malaise, muscle pain, headache, rash, and loss of appetite. Severe reactions usually do not result in long-term problems for the participant, but can cause significant acute illness requiring treatment and hospitalization. They are rarely life-threatening, but can be. These reactions can include severe anaphylactic reactions and seizure.

There may be risks that are not known at this time. If any new risk is reported, the study doctors will let you know as soon as possible.

Blood draw and IV insertion risks: Drawing blood and inserting an IV may cause pain, bruising, lightheadedness, dizziness, possible fainting, local discomfort, bleeding, and, rarely, infection where the needle was inserted.

Risk of Mosquito Feeding

You may have some itching, mild rash, or irritation where the mosquitos bite you. You may need to put some medicated cream or lotion on the area if it bothers you. Rarely, mosquito bites can cause more severe irritation, allergic reactions, or secondary infections at the site of the bite requiring antibiotics.

Urine Drug Tests: To determine if you are eligible for this study, it will be necessary to test your urine for illegal drugs. If your drug test is positive, you will be told that you will not be able to participate in this present study. The results of the drug testing will be noted in your NIH medical record.

POTENTIAL BENEFITS

You will not receive any direct medical benefit for participating in this study. However, what we learn from this study may allow us to further develop a new vaccine for mosquito-borne infections that may benefit others in the future.

ALTERNATIVES TO PARTICIPATION IN THIS STUDY

You may choose not to participate in this study. This will not affect your eligibility to participate in other protocols at the NIH.

USE OF RESEARCH DATA

To advance science, it is helpful for researchers to share information they get from studying human subjects and their data. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the information combined from many studies to learn even more about health and disease.

If you agree to take part in this study, some of your data will be placed into one or more scientific databases after it has been stripped of identifiers such as name, address, and birth date. It may then be used for future research on any topic and shared broadly for research purposes. A researcher who wants to study the information must apply for access to the database. Researchers who are approved to access the database may be able to see and use your information, along with information from many other people. You will not receive direct benefits from future research that uses your data and information.

WITHDRAWAL FROM THE STUDY

You may voluntarily withdraw from this study at any time and withdraw permission for your individual data, specimens, and health information to be used for additional or future research. If you choose, you may request to have your research data destroyed. However, it may not be possible to withdraw or delete data once they have been shared with other researchers. Additionally, you may be removed from the study without your consent. This would be done if it is felt to be in your best medical interest or if the research is stopped. If you leave the study prior to completion, you will be asked to come in for a final study visit.

If you become pregnant during the course of the study, you must inform your doctor and study staff right away. You will be withdrawn from the study. However, with your permission, you will be followed until your delivery.

COSTS TO YOU FOR YOUR PARTICIPATION IN THIS STUDY

There will be no charge to you or your health insurance company for any tests, procedures, or medications directly related to this study.

COMPENSATION

You will be compensated in accordance with Clinical Center guidelines for compensation of healthy volunteers. The compensation will be determined considering your time and the inconvenience of participating in this study, and will also be based on the number of clinic visits and the number of days you are hospitalized and participate in the study. The compensation plan is listed below:

Day 0	$200
Day 7 (± 2 days)	$70
Day 14 (± 2 days)	$70
Day 21 (± 2 days)	$200
Day 28 (± 2 days)	$80
Day 35 (± 2 days)	$80
Day 42 (+ 14 days)	$400
Follow up visits ~60 days (± 14 days) X5	$60x5=$300
Expected total for completion of ALL study visits	*$1,400*
Study-requested interim visits:	$75

The total expected compensation is $1,400 for completion of all study visits as planned. You will be compensated according to the number of visits that you complete.

If deemed medically necessary by the doctor, you may be asked to come in for additional follow-up visits. Reimbursement will be provided for interim visits that are requested by the Principal Investigator but not for interim visits requested by the participant.

STORED SAMPLES AND FUTURE RESEARCH

If you agree to participate in this study, you also agree to let us store your samples for future research. These stored samples may help us learn more about immune response to the vaccine. We will label your stored samples with a code that only the study team can link to you. We will keep any information that can be traced back to you as private as possible. If you change your mind and decide you do not want us to store your samples, please contact us. We will do our best to comply with your request, but cannot guarantee that we will always be able to destroy all your samples.

We might send your samples to other investigators for their research, along with the coded label. We might also share information such as your sex, age, health history, or ethnicity. We will not sell your samples and you will not be paid for any products that result from the research. Some future studies may need health information (such as smoking history or present health status) that we don't already have. If so, our study team will contact you. Future research that uses your samples will probably not help you, but it may help us learn more about how to treat or prevent mosquito-borne and other health problems. In general, the research tests we perform are not like routine medical tests, and may not relate directly to your medical care.

Some of the blood drawn from you as part of this study may be used for genetic tests. Genetic tests can help researchers study how health or illness is passed on to you by your parents or from you to your children. By agreeing to participate in this study, you do not waive any rights that you may have regarding access to and disclosure of your records. For further information on those rights, please contact Dr. Memoli, principal investigator.

Any genetic information collected or discovered about you or your family will be confidential. Records containing this information will be kept on password-protected computer systems and in locked and secured quarters within the Clinical Center. We will not release any information about you or your family to relatives, any insurance company, employer, or your primary care physician without your written permission. When genetic data is shared in databases, even when access is limited to approved users, confidentiality cannot be guaranteed because it may be possible to re-identify the data. Re-identified data could be used to discriminate against or stigmatize you, your family or other groups to which you belong. However, state and federal laws provide some protections against genetic discrimination. Researchers who will have access to genetic information about you will take measures to maintain the confidentiality of your genetic information.

NEW FINDINGS

Any new findings that are discovered during this study, including those that may affect your willingness to continue, will be fully discussed with you.

CONFLICT OF INTEREST

The National Institutes of Health reviews NIH staff researchers on this study at least yearly for conflicts of interest. The following link contains details on this process https://ethics.od.nih.gov/procedures/SOP_21_v3_10-21-14.pdf. You may ask your research team for additional information or a copy of the Protocol Review Guide. This protocol may have investigators who are not NIH employees. Non-NIH investigators are expected to adhere to the principles stated in the Protocol Review Guide.

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Matthew J Memoli, M.D., M.S., at Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, MSC 3203 33 North Dr., Bethesda, MD 20892, through the study team at 301-451-7705 or 301-761-6800, email: holly.baus@nih.gov

You may also call the Clinical Center Patient Representative at (301) 496-2626.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JANUARY 22, 2018 THROUGH JANUARY 21, 2019.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____