Institutional Review Board
Informed Consent Document for Research
MASTER CONSENT

Study Title: A Phase 1, Placebo-Controlled, Double-Blinded Study to Assess the Safety and Pharmacokinetics of Single Ascending Doses of EV68-228-N in Healthy Adult Volunteers
Version Date: 26Jan2024

Part 1 of 2: MASTER CONSENT, Version 2.0

Name of participant: _____ Age: _____

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at more than one location. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
We are inviting you to be in a research study because you are a healthy person and 18-49 years old. You can choose if you want to participate. You do not have to be part of this study. If you agree to be in the study, you will be one of about 36 people who take part in this study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of taking part in this study, you will be told so you can decide whether or not you still want to be in this study.

Why is this study being done? We are testing an antibody called human monoclonal antibody 228 (EV68-228-N), that we think will help fight against a virus called *Enterovirus D68 (EV-D68)*. *EV-D68* has been linked to severe respiratory and neurological disease such as acute flaccid myelitis (AFM). EV-D68 can cause an illness like polio in young children.

Right now, there are no approved treatments to prevent the severe illness EV-D68 can cause.

The main reason for this research study is to assess the safety of a monoclonal antibody against EV-D68 that is called EV68-228-N.

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This study is funded by the National Institutes of Health (NIH), Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID), Infectious Diseases Clinical Research Consortium (IDCRC) and is being conducted at 2 sites in the USA. There will be a total of about 36 people enrolled into this study.

Study Overview

If you agree to take part in this research study, your participation will last for about 4-6 months. You will be randomly assigned by chance to receive an infusion that contains either the antibody (EV68-228-N) or a placebo. There's about an 83% chance that you'll receive the antibody. If you consent to participate, you will come to the clinic for 10 visits, including a screening visit to see if you are eligible to be in the study.

During your study visits you will have:

- physical exams, and we will review your health history
- blood draws and electrocardiograms (ECGs) to make sure you are healthy enough to be in the study and that you remain healthy after the infusion
- one infusion of either antibody (EV68-228-N) or placebo
- blood draws to test how long the antibody stays in your body
- blood draws to test if your body makes its own antibodies against EV68-228-N

There is no direct benefit to you from participating in this study. You will be compensated for your time. You will not have to pay for any of the research tests, study procedures or study product. There are some risks to participating. The main risks are discomfort from the blood draws and the needlestick for the infusion. Other risks include loss of privacy and breach of confidentiality. All the expected risks are listed later in this document.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Purpose of the Research Study

We are testing the safety of a human monoclonal antibody 228 against a virus called Enterovirus D68 (EV-D68) in healthy adults. EV-D68 has been linked to severe respiratory and neurological disease such as acute flaccid myelitis (AFM). EV-D68 can cause an illness like polio in young children. AFM outbreaks

happen all over the world, including in the United States. In the United States, AFM outbreaks happen every other year and around the same time as when people get sick from EV-D68. We now see strong connections between EV-D68 and the presence of AFM and polio-like illness in children.

Right now, there are no approved treatments for preventing the severe illness caused by EV-D68. We need ways to prevent severe illness from EV-D68, and an infusion of an antibody that fights EV-D68 could be one way to do this. An infusion is a slow, steady introduction of a liquid into the body through a vein.

Human monoclonal antibody 228 (EV68-228-N) is an antibody that was developed from patients recovering from EV-D68 disease. Evidence suggests that it can help prevent sickness from EV-D68, including AFM. The main reason for this research study is to assess the safety of EV68-228-N.

We will enroll about 36 people into this study. Three groups of 10 people will receive the EV68-228-N infusion, and three groups of 2 people will receive a placebo alone. The placebo in this study is an infusion that contains no antibodies. There is about an 83% chance of receiving the infusion with the antibody. This will be decided randomly. The study is "blinded" meaning that neither you nor the study team will know if you got antibody or placebo.

To qualify for this study, you are:

- Willing and able to understand and provide written informed consent before starting any study procedures
- 18-49 years old
- Not pregnant and not planning to become pregnant during the study
- Not lactating

To qualify for this study, you agree to:

- For females: Use contraception for the whole study. Study staff will talk with you about acceptable forms of birth control.
- Not donate ova or oocytes during the study
- Not donate blood or blood products during the study

You cannot be in this study if you:

- Are currently enrolled in or you plan to participate in another clinical trial with a study drug that will be received during your enrollment in this study

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- Have a history of major allergies to any of the compounds in the infusion
- Have any history of an infusion reaction to any biologic product
- There are other reasons why you might not be eligible for this study, and the study staff will check for these in the screening process.

To be in the study, you must sign this consent form. You must also be able to:

- Understand, agree to and follow all study procedures
- Come to the clinic for all study visits
- Tell us about any changes in your health or the way you feel
- Tell us if you want to stop taking part in this study at any time

What Are the Risks of This Study?

There are risks to taking part in any research study. There may be adverse events (side effects) not known at this time and/or potentially life-threatening side effects. Additionally, all drugs have a potential risk of an allergic reaction, which if not treated right away, could become life-threatening.

Ask the study clinician if you have questions about the signs or symptoms of any side effects that you read about in this consent form. You should also tell the study clinician or study staff if you have any side effects while participating in this study.

Risks from the EV68-228-N Infusion

This treatment is investigational, which means EV68-228-N has not been approved by the U.S. Food and Drug Administration (FDA). There may be risks that we do not know about at this time. These are not likely to happen, but because there is a possibility, we will keep you at the clinic for about 5 hours after your infusion to check your health.

The infusion will be given to you through a needle inserted into a vein in your arm (also known as an intravenous (IV) infusion). Infusion reactions can occur but are usually mild. These reactions may include low grade fever, chills, rigors, body aches, nausea, vomiting, diarrhea, headache, rapid heart rate, or chest pain. There is also a small chance that you may have an allergic reaction to the infusion product. These symptoms may include dizziness, difficulty breathing, low blood pressure, high blood pressure, itchy skin, hives, a rash, or swelling under your skin.

If these reactions occur, drugs given by study staff can usually stop them. It is expected that these reactions would be mild. Study staff will give you medical help if these or any other side effects should

happen during the study procedures. Most people who experience an allergic reaction completely recover.

It is possible that receiving the study infusion may change how your regular medicines, vaccines, or supplements work. It is very important that you tell the study clinician about any medicines, supplements, or vaccines before you take them during the study.

If you stop or change the amount of your regular medicine, therapy, or supplements to be in the study, your health might get worse. Please tell the study clinician or study staff right away if you have any problems when you stop or change your regular medicine, therapy, or supplements.

Please tell the study clinician or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study. Please let the study staff know about these other problems whether or not you think they are related to the study infusion. Ask the study clinician if you have questions about the signs or symptoms of any side effects that you read about in this consent form.

Risks from Intravenous Catheter, (IV) Placement and Blood Sampling
Placing an IV and doing blood draws may cause some pain when the needle enters your skin. It may also cause some soreness or bruising of the skin for a day or two. Bruising can be prevented or reduced by putting pressure on the skin for a few minutes after the needle is removed. The skin could get infected, but infection is rare. To lower the risk of infection, the study clinician and/or study staff will clean the skin by wiping it with alcohol. The study staff will use clean tools for all study procedures. Very rarely, you could feel dizzy or faint. Please tell the study staff if you feel dizzy or faint so you can lie down while your IV is started and while your blood is drawn.

Risks from Electrocardiograms (ECGs)
You may have redness or a rash on the skin where the adhesive (sticky) pads are placed. This is brief and should not require medical help. You may also experience slight discomfort (like removing a bandage) when the adhesive pads are removed from your skin. There could be a brief loss of personal privacy while the ECG pads are placed on your body. Measures will be taken to ensure your personal privacy is maintained during the placement and removal of ECG pads and during the ECG procedure.

Pregnancy and Breastfeeding

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Because the risks of the infusion to a person who is pregnant and the fetus are unknown, pregnant persons are not allowed to participate. People of childbearing potential will be counseled against becoming pregnant during their participation in the study. If you become pregnant while enrolled in the study and after the infusion, we will ask for your permission to follow up with you on the outcome of your pregnancy. This may last until about 6 weeks after your pregnancy. We will be asking you questions about your health and the health of the fetus and the newborn infant.

Because the impact of the infusion on breastmilk and the risk to breastfeeding infants is unknown, a person who is lactating is not allowed to participate in the study.

Confidentiality
There is a possible risk of loss of confidentiality of your information. Everything will be done to prevent this. You will read more about the protection of your information later in this form.

Potential benefits that might result from this study:
There is no known direct benefit to you for being in this study. We hope the study will teach us more about the EV68-228-N infusion and if we need further study of the infusion. This may help future people who might get sick from EV-D68 and prevent AFM in children.

Study Procedures

During the study, you will come to the clinic for 10 visits, including a screening visit to see if you are eligible to be in the study. You will be randomly assigned by chance to receive an infusion that contains either the antibody or a placebo.

On the day you receive the infusion, you will be in the clinic for about 7-8 hours. On that day, before you get the infusion, you will have an ECG and we will draw your blood. You will get an IV infusion through a needle placed in a vein in your arm. The infusion will take about 15-30 minutes. The study staff will monitor you during the infusion. There will be 4 blood draws after the infusion. Blood may be collected through a second IV site or separate blood draws. You'll also have another ECG about an hour after the infusion is finished. You'll stay at the clinic for about 5 hours after the end of the infusion so study staff can monitor your health. You will be seen in the clinic until all procedures are complete and you are feeling well.

After your infusion, you will come into the clinic 8 more times for follow-up visits to see how you are feeling and to have blood draws. You'll need to come back to the clinic 24 and 48 hours after the time of your infusion because it is very important for seeing how long the antibodies from the infusion stay in

your system. You'll also need to come back at the timepoints 7, 14, 28, 60, 90, and 120 days after the infusion.

During the study, we will collect blood from you 14 times. Some of that blood will be tested to see if the infusion has any impact on the regular amounts of certain compounds in your blood. Some of the blood will be tested to see how long the antibodies stay in your system. Some of the blood will be tested to see if your body makes its own antibodies against EV68-228-N.

For the whole study, the amount of blood collected will be approximately 180mL, which is about 12 tablespoons. This is less than the limit of 36 tablespoons (525 mL) of blood in any 8-week period, which is the amount of blood allowed to be drawn under the American Association of Blood Banks standards.

You will get a handout so you will know what will happen at each study visit. The study staff will explain each visit to you. Study visits are briefly described below.

Screening Visit:

- You will be given a description of this study.
- We will ask you questions about you and your health history. This may include asking your age, race, ethnic group, any past or present illnesses, hospitalizations, surgeries, and medicines you are taking.
- We will go over your medical history and medicines.
- You will have a physical exam.
- You will have an electrocardiogram (ECG).
- We will use a needle to take your blood and test for:
    - Safety labs that tell us how healthy you are
- If you can get pregnant, we will take your urine to conduct a pregnancy test.

Enrollment Visit/Day 1:

- We will go over your medical history and medicines.
- You will have a physical exam.
- We will take your vital signs such as oral temperature, pulse, and blood pressure.
- If you can get pregnant, we will take your urine to conduct a pregnancy test before the infusion. You must have a negative pregnancy test before the infusion.
- You will have an ECG before and after the infusion.
- We will take your blood a total of 5 times.

- You will receive a single infusion of the antibody or placebo.
- We will carefully monitor you during the infusion. You will be on a heart/breathing monitor that displays your pulse and breathing on a screen.
- You will be observed in the clinic for about five hours to complete study procedures.
- We will show you how to use your e-Memory Aid.

Visit 2/Day 2:

- We will review your e-Memory Aid.
- We will go over your medical history and medicines.
- You will have a physical exam.
- You will have an ECG.
- We will use a needle to take your blood. We would like this blood draw to be as close as possible to 24 hours from the start of the prior day's infusion.

Visit 3/Day 3

- We will review your e-Memory Aid
- We will go over your medical history and medicines.
- You will have a physical exam.
- We will use a needle to take your blood. We would like this blood draw to be as close as possible to 48 hours from the start of the infusion.

Visit 4/Day 8

- We will review your e-Memory Aid
- We will go over your medical history and medicines.
- You will have a physical exam.
- We will use a needle to take your blood.

Visit 5/Day 15

- We will go over your medical history and medicines.
- You may have a physical exam.
- We will measure your temperature, pulse and blood pressure.
- We will use a needle to take your blood.

Visit 6/Day 29

- We will go over your medical history and medicines.

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- You may have a physical exam, if needed
- We will measure your temperature, pulse and blood pressure.
- We will use a needle to take your blood.

Visit 7/Day 61 and Visit 8/Day 91

- We will ask you about your health since the last time we saw you.
- You may have a physical exam, if needed.
- We will use a needle to take your blood.

Visit 9/Final Study Visit/Day 121

- We will ask you about your health since the last time we saw you.
- You may have a physical exam, if needed.
- We will use a needle to take your blood.

	Screening Visit	Enrollment Visit	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Final Visit
		Day 1	Day 2	Day 3	Day 8	Day 15	Day 29	Day 61	Day 91	Day 121
Infusion		X								
Review medical history	X	X	X	X	X	X	X	X	X	X
Physical exam	X	X	X	X	X	If needed	If needed	If needed	If needed	If needed
Blood draw	1TB	3TB	1TB	1TB	1TB	1TB	1TB	1TB	1TB	1TB
ECG	X	X[a]	X							
Pregnancy test	X	X								

a) Two ECGs will be done on Day 1 about 15 minutes before infusion and one hour after infusion.

Early Termination & Unscheduled Visits

If you decide to stop taking part in the study or the study clinician withdraws you, we may ask you to come to the clinic for a final visit and a final blood draw. If you miss a study visit or you don't feel well between study visits, let us know. We may ask you to come to the clinic for an unscheduled study visit.

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Other Options

Your participation in this research study is up to you. Take all the time you need to make your choice. If you decide to be in this study, you may change your mind at any time. You can stop being in the study and we will still take good care of you. You can ask questions at any time. It is also okay to ask more questions after you decide to be in the study. You will not be penalized or lose benefits you already had if you refuse to take part in this study.

Stopping the Research Study Early:
If you choose to stop taking part in the study, we will ask you to come to the clinic for one more visit. We will review your information and the study clinician may want to give you a physical exam. Your study clinician may also want to perform other tests such as a blood draw or ECG to ensure you are healthy.

If you stop early, no added information will be collected from you. However, information already collected from you will be saved and may be included in the study report. Your personal information will remain private and will not be shared in the study report or any publications related to this study.

If we find out new information about the infusion, we will tell you. You can then choose if you want to stay in the study.

During the study, it is also possible that:

- You are removed from the study for your safety.
- The study may be stopped.

Reasons why the study clinician may take you out of this study:

- You become pregnant prior to study infusion
- You no longer meet eligibility criteria
- You meet individual halting criteria
- You are unable to adhere to the study schedule

- You develop a medical disease or condition, or new clinical finding(s) for which continued participation, in the opinion of the study clinician might threaten your safety, prevent your successful completion of this study, or interfere with your evaluation of responses
- We are unable to reach you

Clinical Trials Registry

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality and privacy

Certificate of Confidentiality:

To help us protect your privacy, we have a Certificate of Confidentiality (Certificate) from the NIH. Study staff cannot provide to any person not connected with the research your name, or any materials that contain identifiable, sensitive information about you, unless permitted by a legal exception, such as state laws that require reporting of some contagious diseases. The most important protection provided by the Certificate is that the study staff cannot be forced to provide any of your identifiable, sensitive information, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, such as if there is a court subpoena, without your permission.

The study team will use the Certificate to resist any demand for information that would identify you.

Your information protected by the Certificate may still be disclosed or used when the information:

1. Is disclosed to people connected with the research; for example, information may be used for auditing or program evaluation internally by the NIH; or
2. Is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the FDA. This does not include disclosure for use during legal proceedings as noted above;
3. Is necessary for your medical treatment and you have consented to this disclosure;
4. Is for other scientific research as allowed by applicable federal regulations;
5. Is disclosed with your consent.

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The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing and dating below you consent to those disclosures.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. The Certificate does not prevent you from sharing any information you want to with someone else.

Privacy
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

No genetic tests will be performed on samples/specimens. Each sample/specimen will be encoded (labeled) only with a barcode and a unique tracking number that connects to a code key at the study site. Restricted access to the code key is maintained by the study clinician to protect your confidentiality. Reports from future research studies performed using your samples/specimens will NOT be kept in your health records.

Secondary Research
After all tests required for this study are done, we will save leftover samples for possible secondary research instead of throwing them away. Secondary research is research that is not part of this study but will be performed in the future. You will not be told about the secondary research, and you will not be notified of any results from future research.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Samples saved for secondary research will be stored indefinitely at a central clinical storage facility with IRB oversight. Samples will only be labeled with a barcode and an ID (not with your name, initials, or any other information that could readily identify you). These samples saved for secondary research could be used for secondary research studies or distributed to another investigator for secondary research studies without additional informed consent. If these samples are tested in the future, the results may

be published. You will not be identified in such publication. In other words, the publication will not have any information about you that would enable someone to determine your identity.

There are no benefits to you in the collection, storage and secondary research use of your samples. The results of any future research testing will be kept confidential in the same way as the results of other testing done for this study. The results of any future research will not be available to you or your regular clinician and will not be placed in your medical record.

Study Results:
Records identifying you will be kept confidential, and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the research study are published, your identity will remain confidential. You will not be contacted to inform you of the research results unless there are any safety issues.