Trial Readiness in Cavernous Angioma with Symptomatic Hemorrhage (CASH)

NCT03652181

FUBV Model Consent
IRB approved May 21, 2021

RESEARCH PARTICIPANT INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title: Trial Readiness in Cavernous Angiomas with Symptomatic Hemorrhage (CASH)

Follow-Up Biomarker Validation (FUBV) Consent

Application No.: IRB00170076

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See "Study Site Information" page(s) near the end of this consent form for contact information for your local study team.

This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this informed consent form includes two parts. The first part of this document includes information that applies to all study sites. The second part of the consent form includes information specific to the study site where you are being asked to enroll.

What you should know about this study:

- You are being asked to participate in a research study.
- This consent form explains the research study and will give you information about the study to help you decide whether you want to participate. You may choose not to take part in the study or may choose to leave the study at any time.
- Please read it carefully and take as much time as you need to fully understand the study and the consent form.
- Please ask questions at any time about anything you do not understand. During the study, we will tell you if we learn any new information that might affect whether you wish to continue to be in the study.
- Ask your study doctor or the study team to explain any words or information in this informed consent that you do not understand.

Why is this research being done?

The purpose of this research study is to study patients with cerebral cavernous malformation (CCM) disease who have had a symptomatic hemorrhage (CASH) in the past year. There are fewer than 200,000 cases of brain cavernous angiomas (CA) in North America today who have suffered a symptomatic hemorrhage (SH). While much progress has been made in understanding the natural history of CAs, there is still much to learn. To continue these efforts, a strong group effort of researchers in this disease and a very engaged patient advocacy and support group, the Angioma Alliance are actively involved. This research study is being done to help determine (1) the feasibility of screening, enrollment rates, baseline disease categorization and follow-up of CASH patients, (2) the reliability of advanced imaging biomarkers at multiple sites, and (3) the rates of recurrent hemorrhage (bleeding) and change in functional status, quality of life and biomarker measurements during prospective follow-up.

How many people will be in this study?

This study is being conducted at several hospitals in the United States simultaneously. Up to 200 participants are needed to complete this study. Of those 200 participants, approximately 120 will take part in the follow-up imaging studies. You are part of the group who will take part in follow-up studies.

What will happen if you join this study?

If you agree to be in this study, the following things will happen:

NOW, AT THE SCREENING VISIT:

- You will be given the informed consent to review and ask questions. If you agree to be part of the study, we will review your medical and CCM disease history and any symptoms you have had in the past year. We will perform standard neurological assessments, the modified Rankin Score (mRS), the NIH Stroke Scale (NIHSS), a health related quality of life (EuroQoL) assessment and an assessment of anxiety, depression, and fatigue (PROMIS29). You will have a physical exam (height, weight and vital signs) and your scheduled MRI scan as part of your standard care. In addition, you will be in the MRI scanner for an additional 15 minutes while we do some extra research images (scans). These extra images are for research only and will not be used for your medical care. You will not receive any additional contrast (dye) for these extra images. This visit will last approximately 2 hours, including time for your MRI.

ONE YEAR FOLLOW-UP

- Approximately one year from now, you will return to clinic and we will review your medical and CCM disease history and any symptoms you have had in the past year. We will perform standard neurological assessments, the modified Rankin Score (mRS), the NIH Stroke Scale (NIHSS), a health related quality of life (Euro-QoL) assessment, and an assessment of anxiety, depression, and fatigue (PROMIS29). You will have a physical exam (height, weight and vital signs) and your scheduled MRI scan as part of your standard care. In addition, you will be in the MRI scanner for an extra 15 minutes while we do some additional research images (scans). These extra images are for research only and will not be used for your medical care. You will not receive any additional contrast (dye) for these extra images. This visit will last approximately 2 hours, including time for your MRI.

TWO YEAR FOLLOW-UP

- Approximately two years from now (about 12 months from the one year follow-up appointment), you will return to clinic and we will review your medical and CCM disease history and any symptoms you have had in the past year. We will perform standard neurological assessments, the modified Rankin Score (mRS), the NIH Stroke Scale (NIHSS), a health related quality of life (Euro-QoL), and an assessment of anxiety, depression, and fatigue (PROMIS29). You will have a physical exam (height, weight and vital signs) and your scheduled MRI scan as part of your standard care. In addition, you will be in the MRI scanner for an extra 15 minutes while we do some additional research images (scans). These extra images are for research only and will not be used for your medical care. You will not receive any additional contrast (dye) for these extra images. This visit will last approximately 2 hours, including time for your MRI. This is your final study visit.

In the future, identifiers associated with your data could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers without notifying you or asking your permission for this use.

The results from this study will not be shared with you.

What are the risks or discomforts of the study?

Your standard of care MRI requires the use of contrast dye. As part of this research study, you will be in the MRI scanner for an extra 15 minutes for the additional research images (scans). You will not get more contrast dye for the extra images. As usual, the dye will be given intravenously (through a vein). There may be some mild discomfort or bruising at the intravenous site and a minimal risk of local infection which would generally be treated with oral antibiotics. Other side effects of the contrast agent are extremely rare but include nausea, paresthesias (itching, tingling, or pickling of the skin), headache and dizziness. Hemolysis (breakdown of blood cells) has been reported following contrast administration in patients with sickle cell disease and patients with other hemolytic anemias (low red blood count in body). The use of intravenous contrast agents will not be permitted if you have either of these conditions or if you are pregnant, since the effect of the contrast dye on an unborn child is unknown.

Likely: Some subjects may experience claustrophobia or a “closed-in” feeling.

Less likely: When very high speed methods are used for imaging, some people experience a mild twitching sensation. This should not be uncomfortable, but let us know if you experience this sensation since we can modify the imaging method to eliminate it.

The risks associated with the use of the radio antenna (RF coil) are minimal. There is a minimal risk of skin burns if the coil is used improperly. The MRI staff is fully trained in the proper use of these devices.

Rare but serious: In addition to the above, in relation to the gadolinium-based contrast agent: a condition called Nephrogenic System Fibrosis/Nephrogenic Fibrosing Dermopathy (NSF/NFD) has been reported in patients with moderate to end-stage kidney disease who receive gadolinium contrast agent. Symptoms of the disease include itching, hardening and tightening of the skin; yellowing of the eyes; and pain, stiffness and limited range of motion in the joints and muscles. Notify your doctor if you have kidney disease or you have had a liver transplant. The health of your kidneys will be checked by finger prick tests.

This study involves the potential risk of a loss of privacy due to collection of identifying personal information that will be used to identify the appropriate scans. This risk will be minimized by deletion of all identifying information before releasing the images to the research team from the radiology department. Your scan will be assigned a study number, with the list of patients/numbers being kept on a password-protected computer with limited access. This information will be entered into a secure database at the Data Coordinating Center at Johns Hopkins University.

Are there risks related to pregnancy?

We do not know if MRI scans are safe during pregnancy, so if you think you might be pregnant, you should not be in the study.

Are there benefits to being in the study?

There will be no direct benefits to subjects participating in this study. However, the information gained from this study may lead to successful clinical trials testing novel therapies in patients with cerebral cavernous angiomas.

What are your options if you do not want to be in the study?

You do not have to join this study. If you do not join, your care will not be affected in any manner.

Will it cost you anything to be in this study?

There will be no costs to you or your insurance company resulting from your participation in this research study. The research study will pay for the additional MRI images. However, you or your insurance company will be responsible for costs related to your usual medical care.

Will you be paid if you join this study?

You will not be paid if you join this study, but if you are eligible to enroll, you will receive a stipend for each study visit that you complete to help cover any costs for travel, lodging, and/or services that are required for you to complete the study visits. If you are traveling less than 200 miles to the enrolling site, you will receive $50 per visit (baseline, Year 1, Year 2). If you are traveling more than 200 miles to the enrolling site, you will receive $500 per visit (baseline, Year 1, Year 2). You will receive reimbursement 4-6 weeks after completing each study visit.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments exceed $600 per year, these payments will be reported to the Internal Revenue Service and you will receive a 1099-MISC form to process when you file your yearly tax returns.

Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting usual regular medical care.
- If you leave the study early, we will keep information already collected for the study or any follow-up activities. No new information will be collected.

Why might we take you out of the study early?

You may be taken out of the study if:

- The study is cancelled or stopped early.

- There may be other reasons to take you out of the study that we do not know at this time.
- If you are taken out of the study early, we will keep information already collected for the study or any follow-up activities. No new information will be collected.

How will your privacy be protected?

The research team working on this study will collect information about you. This includes things learned related to the study as described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at this hospital, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety. Sometimes other people at this hospital may see or give out your information. These include people who review the research studies, their staff, lawyers, or other staff at this hospital.

Your hospital, the Data Coordinating Center (Johns Hopkins University) and the Clinical Coordinating Center for this study (University of Chicago) have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. Federal regulations require that certain information about individuals be kept confidential. This information is called "protected health information" (PHI). PHI includes information that identifies an individual personally such as name, address and social security number, or any medical or mental health record, or test result, that may have this sort of information on it. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. The laws state that people may see and review their medical records at any time. However, in a research study, people may not see the study results or other data about the study until after the research is completed unless the study doctor decides otherwise. By signing this form you provide your permission, called your "authorization", for the use and disclosure of information protected by the Privacy Rule.

People outside of this hospital may need to see or receive your information for this study and by law must protect it. This is to ensure that the study is being conducted correctly, safely, with your information properly stored and protected.

PHI collected during this study may also be shared with the following entities that, while not obligated by law to protect PHI, will protect it to the best of their ability:

- The funding partner – National Institute of Neurological Disorders and Stroke (NINDS)
- The Food and Drug Administration (FDA)
- Research Monitors hired by the sponsor to oversee the study and review medical records to ensure study-related information is correct
- With any person or agency required by law

Some of the information collected for this study will be sent electronically to the research center at JHU and will become part of the study database. This information will include your PHI, such as your name, address, date of birth and your health information. Your PHI needs to be shared with JHU in order to check that the information collected about you for the study is correct. These data records that include your PHI will be sent to JHU using a secure method (an encrypted transmission) and will be stored on a secure server that may only be opened and read by a limited number of individuals with permission to do so. Your PHI will be maintained in the JHU database until the study is permanently closed. There is no expiration date as to how long your data will be archived.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed. We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

The authorization to use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are listed at the end of this consent document.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

What other things should you know about this research study?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed on the Study Site Information page(s) near the end of this consent form.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies to protect the rights and welfare of the people taking part in those studies. The IRB for this study is the Johns Hopkins Medicine IRB. You may talk to them at 410-955-3008 if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject**.**

Other Databases

If you agree to take part in this study, the information collected for this study will be placed into one or more scientific databases. In particular, the National Institutes of Health maintains a database. The NIH database is a restricted database, meaning a researcher who wants to study information must work with the group overseeing the database to obtain the information. Security measures are in place to protect these data.

Researchers with an approved study will be able to see and use some of your information, but your name and other information that could directly identify you (such as your name or address) will not be placed into the database. There is no direct benefit to you that is expected from any secondary research that may be conducted.

If you decide to withdraw from the study as outlined in the following section, your data will be withdrawn from these databases. However, if your data have already been submitted to an NIH database and distributed to other researchers, or your data have been de-identified and can no longer be linked back to you, your data will not be able to be withdrawn.

Certificate of Confidentiality

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

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. Disclosures that you make yourself are also not protected.

What happens to Data that is collected in the study?

The data collected from you during the study are important to both this study and to future research and will be stored in a safe, secure location both at this hospital and at the Data Coordinator Center at JHU.

If you join this study:

- You should understand that you will not own the data, and should researchers use the data to create a new product or idea, you will not benefit financially.
- With appropriate protections for your privacy, both researchers at your hospital and partners in research at other hospitals may study your data.
- If any data is in a form that identifies you, researchers may only use them in future research with your consent or IRB approval.
- You will not own any product or idea created by the researchers working on this study.
- You will not receive any financial benefit from the creation, use or sale of such product or idea.

During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

Often it is helpful for scientists to share information they get from studies in order to learn more about health and disease. The data from this study will be kept in a central data capture system and will be accessible by all participating study sites. The data may include health information and images (for example, laboratory results). Results of this study will also be published in a medical journal(s).

Your name and any other identifying information will NEVER be included in information that is published in a medical journal(s) or sent to a databank(s) (this is called de-identification). Researchers ALWAYS have a duty to keep your information confidential.