FITCH trial

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Wake Forest®
School of Medicine

Department of Neurosurgery

SELECTIVE IMMUNOMODULATION IN THE TREATMENT OF CEREBRAL EDEMA AFTER INTRACEREBRAL HEMORRHAGE

Informed Consent Form to Participate in Research

Stacey Quintero Wolfe, MD, Principal Investigator

SUMMARY

You are invited to participate in a research study. Research studies are designed to gain scientific knowledge that can be used in the future to help other people. The purpose of this research study is to assess the safety of a medication, fingolimod, to treat brain swelling because of bleeding in the brain, also called intracerebral hemorrhage or ICH. You are invited to be in this study because you have experienced an intracerebral hemorrhage, or ICH. Your participation in this research will involve the same care and follow-up appointments that all patients with intracerebral hemorrhage undergo. This involves your hospital stay and 4 follow up visits – one at 30 days, 3 months, 6 months and the final visit at 12 months after your hospitalization.

This study is designed to find out if it is safe to give a medication, fingolimod, to treat inflammation, or swelling, that occurs due to the bleeding you experienced in the brain. Participation in this study will involve all standard of care management of your blood clot in addition to a single dose of study medication. Standard therapy for blood clots in the brain may involve standard ICU care, standard medical therapies, and/or if needed, a standard of care placement of a drain (external ventricular drain – EVD) for enlargement of the fluid-filled spaces (ventricles) in the brain, known as hydrocephalus, to drain cerebrospinal fluid (body fluid found in the brain and spinal cord) with the goal to decrease pressure in your brain.

Regarding the dose of medication, there is a risk of side effects, all of which occur in < 1% of people who take the medication on a regular everyday basis, including: temporary slowing of the heart rate, increase in risk of infections, macular edema (swelling of the part of the eye responsible for detailed vision) which is reversible, liver problems, headache, diarrhea, cough, sinus inflammation, back pain, abdominal pain, or pain in arms and legs. There is a 0.5% chance of a serious side effect, including progressive multifocal leukoencephalopathy (very rare brain infection), posterior reversible encephalopathy syndrome (swelling and narrowing of the blood vessels in the brain that can lead to stroke). Because this study is evaluating the safety of a medication that could treat the inflammation that occurs because of bleeding in the brain, you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you to treat your brain bleeding. Other choices may include standard medical management without receiving this medication or surgical removal of the blood clot if it is considered necessary. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Dr. Stacey Wolfe. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is:

Dr. Stacey Wolfe
[redacted]

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at 3[redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have bleeding in the brain, also called intracerebral hemorrhage or ICH. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to test the safety of the medication fingolimod as a potential agent to treat the inflammation caused by brain bleeding in combination with standard clinical care. The goal is to see what effects (good and bad) it has on you and your condition.

The rate of death in patients with ICH despite best medical management remains very high. Also, the rate and amount of recovery is variable. Although the ICH itself can cause damage to brain structures, the swelling because of an inflammatory response to the blood in the brain can cause further significant injury to the brain, leading to worse neurologic problems and less recovery in the future. But there have been recent studies that show that if the swelling can be reduced after ICH has occurred, the rate and amount of recovery can be improved.

Fingolimod has been approved by the US Food and Drug Administration (FDA) to treat the inflammation that causes multiple sclerosis, but it has not been approved for use in the treatment of inflammation due to ICH. In this study, fingolimod will be compared to a placebo. A placebo is a substance, like a sugar pill, that is not thought to have any effect on your disease or condition. In this study, you will either receive the active study medication, fingolimod, or placebo which is not active. Placebos are used in research studies to see if the drug being studied really does have an effect.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?
A total of 30 people at 1 research site will take part in this study. All 30 subjects will be from Wake Forest Baptist Health. In order to identify the 30 subjects needed, we may need to screen as many as 60-70 potential subjects because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?
If you take part in this study, you will have the following tests and procedures:

Screening: With your consent, we will review all of the information used to treat your condition to find out if you are eligible for this study.

- At the time of your admission to the hospital, a standard of care CT scan will be done to confirm the diagnosis of ICH. A CT scan is a test that produces an image of your body using a small amount of radiation. The image shows the body tissues and structures in three dimensions ("3-D"). These CT scans may already have been done per standard clinical care.

- A MRI (magnetic resonance imaging) scan and a MRA (magnetic resonance angiogram) or a CTA (computed tomography angiogram) will also be done. These procedures are part of the standard clinical care to see if the bleeding is caused by abnormal blood vessels, such as an aneurysm (thinning of the wall of an artery), arteriovenous malformation (tangle of blood vessels), or tumor. If this is the cause of your bleeding, you will not be eligible for this study.

- A pregnancy test will be done if you are a female of childbearing potential. This test is part of standard clinical care. You must not be pregnant to be in this study.

- Standard of care speech and swallow evaluation will be done to test your ability to swallow. This can be done at the bedside by a nurse. If you are having trouble swallowing, you will get a nasogastric tube or Dobhoff feeding tube as part of standard of care. The purpose of these devices is to help deliver medications and nutrition directly to your stomach until you recover and are able to safely swallow on your own.

Randomization:
If you are found to be eligible for this study, you will be randomized into one of the study groups below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being in any group. You will either continue to receive standard medical care with a placebo, or you will receive standard medical care with the study drug fingolimod.

Neither you nor the investigator will know which study drug you are receiving. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

Standard medical care plus placebo: if you are randomly assigned to continue to receive standard medical care and placebo:

- You will be given a single dose of the placebo, which will look, taste, and smell exactly like the study drug. If you are unable to swallow, this will be given through the nasogastric tube or Dobhoff feeding tube.
- You will then be taken to the intensive care unit as part of standard clinical care.
- Your vital signs, such as heart rate, blood pressure, temperature, and neurological condition will be monitored daily for the next 6 days. This is done as part of standard clinical care but will be reviewed for study purposes.
- If you require cerebrospinal fluid drainage as part of your clinical care, this procedure will be performed in the Neuroscience Intensive Care Unit. This will involve the placement of a catheter that is less than 1 centimeter in diameter through the brain into the fluid filled spaces (ventricles) in the brain, and this will allow for constant pressure monitoring of your brain, as well as drainage of cerebrospinal fluid. A 5 teaspoon sample of this will be store for future testing of the immune cells and the proteins produced after ICH on Day 1, 3, 5-7 and 10-14 only while the fluid drain is in place. If you do not require cerebrospinal fluid drainage, cerebrospinal fluid will not be collected and stored.
- A standard CT scan will be done on Day 1 after your admission to make sure the bleeding has stopped as part of standard of care, but it will also be reviewed for study purposes to follow the swelling of the brain.
- On Day 3 after your admission, you will also get a standard of care MRI of the brain to evaluate the swelling of the brain. This does not involve radiation or contrast, and carries minimal risk.
- Standard of care blood samples, about 2 tablespoons worth of blood, will be drawn from a vein daily for the first 7 days to monitor natural chemical levels in the blood related to the bleeding in your brain. As part of this study participation, on Days 1, 3, and between 5-7 after taking the medication, a half of the blood that is already drawn (1 tablespoon) will be sent off for testing of the different white blood cells that are affected by the medication. If you are still hospitalized 10-14 days after taking the medication, we will collect another 1 tablespoon worth of blood to send off for testing of the different white blood cells. A small amount of the blood collected will be stored for future tests to analyze the different immune cells and the proteins that can be made by these cells. In the future, research on your specimen may involve whole genome sequencing. However, if you have low blood counts, we will not be collecting your blood.

Standard medical care plus study drug: if you are randomly chosen or assigned to the group that will get the study drug:

- You will be given a single dose of the study drug fingolimod, 0.5 mg, by mouth. If you are unable to swallow, this will be given through the nasogastric tube or Dobhoff feeding tube.
- You will then be taken to the intensive care unit as part of standard clinical care.
- Your vital signs, such as heart rate, blood pressure, temperature, and neurological condition will be monitored daily for the next 6 days. This is done as part of standard clinical care but will be reviewed for study purposes.
- If you require cerebrospinal fluid drainage as part of your clinical care, this procedure will be performed in the Neuroscience Intensive Care Unit. This will involve the

placement of a catheter that is less than 1 centimeter in diameter through the brain into the fluid filled spaces (ventricles) in the brain, and this will allow for constant pressure monitoring of your brain, as well as drainage of cerebrospinal fluid. A 5 teaspoon sample of this will be store for future testing of the immune cells and the proteins produced after ICH on Day 1, 3, 5-7 and 10-14 only while the fluid drain is in place. If you do not require cerebrospinal fluid drainage, cerebrospinal fluid will not be collected and stored.

- A standard CT scan will be done on Day 1 after your admission to make sure the bleeding has stopped as part of standard of care, but it will also be reviewed for study purposes to follow the swelling of the brain.
- On Day 3 after your admission, you will also get a standard of care MRI of the brain to evaluate the swelling of the brain.
- Standard of care blood samples, about 2 tablespoons worth of blood, will be drawn from a vein daily for the first 7 days to monitor natural chemical levels in the blood related to the bleeding in your brain. As part of this study participation, on Days 1, 3, and between 5-7 after taking the medication, a half of the blood that is already drawn (1 tablespoon) will be sent off for testing of the different white blood cells that are affected by the medication. If you are still hospitalized 10-14 days after taking the medication, we will collect another 1 tablespoon worth of blood to send off for testing of the different white blood cells. A small amount of the blood collected will be stored for future tests to analyze the different immune cells and the proteins that can be made by these cells. In the future, research on your specimen may involve whole genome sequencing. However, if you have low blood counts, we will not be collecting your blood.

Study follow up visits: Study participants will be followed for 12 months after surgery.

- You will be asked to return to the clinic at 30-45 days, 3 months, 6 months, and 12 months from today. At these standard of care follow up visits, your neurological condition and blood pressure will be checked and you will be asked questions about how well you are doing. You will also be asked if you are experiencing any side effects or problems from the medication. Standard of care Neuroimagingwill be performed at the 3, 6v and 12 month visits to check for brain swelling and fluid buildup. This is a necessary part of standard care for this problem. You may be asked to undergo another blood sample for laboratory testing and storage for future analysis at the 30 day visit.
- At each of your study follow up visits at 30-45 days, 3 months, 6 months, and 12 months, you will undergo a set of assessments to check different aspects of your recovery. We will evaluate your ability to take care of yourself at home or if you require assistance at home or your facility. We will also test your thinking and memory, and we will be asking if there are changes in your mood since your ICH.

We can send copies of your test results to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study. As part of this study, as mentioned in the next section, we will be asking questions regarding your mental health. If you indicate any feelings of depression or desire to harm yourself or others, per our institution protocol, we will be sharing this information with your physician to appropriately address these concerns.

Storage of Biological Tissue

If you agree to participate in this study, we will collect a total of 5 tablespoons of blood, and possibly a total of 3 tablespoons of cerebrospinal fluid (if your condition requires a spinal fluid drain) to use for future research. These samples will be kept and may be used in future research to learn more about other diseases. Your samples will be obtained by the Department of Neurosurgery and Center for Precision Medicine at Wake Forest University Baptist Medical Center. The samples will be stored in Dr. Timothy Howard's laboratory on the third floor of the NRC and it will be given only to researchers approved by Stacey Wolfe, MD. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. You are not required to provide samples for future research in order to participate in this study.

The research that may be performed with your blood and cerebrospinal samples is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood and cerebrospinal samples will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood and cerebrospinal samples will not affect your care.

Your blood and cerebrospinal samples will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

Your cerebrospinal fluid and blood samples will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.
In addition, de-identified information regarding your DNA and clinical information will be sent to the National Institute for Health's or equivalent database of genotypes and phenotypes (dbGaP) after genome-wide analysis and will be shared with other investigators for research purposes. DNA and information sent to these databases will help researchers better understand how genes affect the risk of developing diseases such as asthma, cancer, diabetes, and heart disease and may lead to better methods to select the best treatment options. Before your information is sent to the dbGaP data repository, it will be de-identified, which means that we will remove any identifying information such as your name, date of birth, address, etc. Thus, researchers using your DNA and clinical data will not be able to link this information back to you.

In the future, people who do research may need to know more about your health. While the study

investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

HOW LONG WILL I BE IN THE STUDY?
You will be in the study for about 12 months.

You can stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

WHAT ARE THE RISKS OF THE STUDY?
Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the drug (fingolimod) we are studying include:

Common side effects:

- Risk of side effects from the medication, all of which occur in < 1% of people who take the medication on a regular everyday basis for > 2 months: temporary slowing of the heart rate, increase in risk of infections, liver problems or temporary abnormal liver tests, increased blood pressure, headache, diarrhea, cough, sinus inflammation, back pain, abdominal pain, or pain in arms and legs.

Rare:

- Risk of serious side effects occurring in < 0.5% of people who take the medication on a regular everyday basis for > 2 months: lymphoma (blood cancer), progressive multifocal leukoencephalopathy (very rare brain infection), posterior reversible encephalopathy syndrome (swelling and narrowing of the blood vessels in the brain that can lead to stroke), macular edema (swelling of the part of the eye responsible for detailed vision) which is reversible, or shortness of breath.
- Death

Discomforts:

- You may experience discomfort that is part of the routine medical care for participants with your condition in the intensive care unit.
- During the follow up visits, you may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any questions you do not want to answer.

There may be side effects and discomforts that are not yet known.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and

any medical conditions you have. This may help avoid side effects, interactions and other risks.

The risk associated with gene analysis studies would be the loss of confidentiality of the results. Your information and sample that are shared with other researchers for future uses, are coded so that the researchers have no known way to know the sample and information are yours except if they were to compare the DNA to another DNA sample provided by you. Unless required by law, we will not release information that identifies you to other researchers without your written permission. A federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information:

-Health insurance companies may not request or use individual genetic information that we get from this research when making decisions regarding eligibility or premiums.

-Employers with 15 or more employees may not use genetic information from this research when making a decision to hire, promote, or fire or when setting the terms of your employment.

Be aware that this new law does not protect you against discrimination on the basis of your genetic information by companies that sell life insurance, disability insurance, or long-term care insurance. There is a risk that being in a genetics study can cause psychological distress or tension with other family members, or that broad data sharing could risk identification of populations or groups. There are no plans to provide you with the results of the gene analysis. Clinical and genetic data may be kept anonymously in a public database. There is always some risk that even de-identified information might be re-identified, however extensive efforts are made by all study personnel to ensure confidentiality of all subjects.

If you are randomized to the study group that receives the placebo, you will not be at risk for increased brain swelling compared to what has already been reported in other studies. You will be at the same risk of developing an infection in the hospital compared to what has already been reported in other studies.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

As part of this study, you will be asked questions about your mood, sleeping patterns, appetite, energy level, ability to concentrate, your level of interest in activities and hobbies, and if you have any thoughts of being hopeless or hurting yourself. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities.

You may experience discomfort, bruising and/or bleeding where the needle is inserted for blood draws. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

Reproductive Risks and other Issues to Participating in Research

Standard of Care follow up for your ICH includes monitoring your condition with CT scans. We will also be collecting blood samples at these follow up visits. The drug fingolimod may take up to 2 months to completely clear from your body, and there is potential risk to a baby if the drug is still in your system. Due to unknown risks and potential harm to the unborn fetus from the CT scans and medication or the inflammatory processes that may be identified in the blood collection, sexually active women of childbearing potential are recommended to use a reliable method of birth control while during their follow up period for their ICH and while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

If you become pregnant during the 6 month follow up period, we will ask you to complete the interviews and questionnaires, but you will not have the CT scans done.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefit of participating in this study may be less inflammation or brain swelling from ICH after administration of fingolimod, which could lead to better neurologic recovery.

Based on experience with fingolimod in patients with multiple sclerosis, animal models of ICH, and a small clinical trial using fingolimod to treat the inflammation after ICH, researchers believe that this medication may be beneficial to subjects with your condition. Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment for your ICH. You should talk to your doctor about all the choices you have. Currently, there are 2 standard of care options to treat ICH. Instead of being in this study, you have these options:

The first option is standard medical management without the use of the study medication. You will be observed and any causes of your ICH will be treated with standard of care medications. Swelling of the brain will be treated with standard medications commonly used in treating the swelling as much as is possible.

If you require surgery, standard surgical removal of the blood clot can be performed without additional administration of any study medication to treat the inflammation.

WHAT ARE THE COSTS?
All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?
The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

The purpose of this research study is to obtain data or information on the safety and/or effectiveness of fingolimod (Gilenya); the results will be provided to the sponsor, the Food and Drug Administration, and other federal and regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

WILL YOU BE PAID FOR PARTICIPATING?
You will receive no payment or other compensation for taking part in this study.
The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?
This study is being sponsored by Wake Forest University Health Science. The researchers do not, however, hold a direct financial interest in any sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security

number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Stacey Wolfe at [redacted] (after hours numbers [redacted]).

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** name, date of birth, phone numbers, medical record numbers, date of surgery, and medical conditions.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups, it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Stacey Wolfe that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Stacey Wolfe
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form, you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://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.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A Wake Forest Baptist Health (WFBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the WFBH medical record, along with any routine medical test results that were obtained at WFBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because:

- Staying in the study would be harmful.
- You need treatment that is not allowed in the study
- Your condition worsened
- You failed to follow instructions
- The study is cancelled
- There may be other reasons to take you out of the study that we do not know at this time.

Information that identifies you may be removed from the materials collected from this study, and may be used for future research without additional consent from you.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Stacey Wolfe, MD at [redacted]. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent: _____ Date: _____ Time: _____ am pm

OR

Legally Authorized Representative Name (Print):_____

The above named Legally Authorized Representative has legal authority to act for the research subject based upon (specify health care power of attorney, spouse, parent, etc.)

Relationship to the Subject: _____

Legal Representative Signature: _____ Date: _____ Time: _____ am pm