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Wake Forest®
School of Medicine

Department of Orthopaedic Surgery

THE USE OF LIPOSOMAL BUPIVACAINE (EXPAREL®) IN SOFT TISSUE SARCOMA RESECTION – CCCWFU 71118

Informed Consent Form to Participate in Research
Cynthia Emory, MD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to see if a medication called liposomal bupivacaine (EXPAREL®) can reduce the pain patients have after surgery to remove a tumor called a soft tissue sarcoma. You are invited to be in this study because you have a soft tissue sarcoma that requires removal by surgery.

If you participate in this research, you will have the same surgery that you normally would have. The difference would be that after your surgery we will give you a drug called EXPAREL®. We will inject it around where the sarcoma was removed. After surgery and while you are at the hospital, we will collect information from you about your pain and recovery. After you leave the hospital, we will follow you for 6 weeks to monitor your progress.

All research studies involve some risks. A risk to this study that you should be aware of is the slight possibility of risk or side effects associated with the use of the medication. This study involves a minor increase in risk compared to the care that is normally given. You should discuss any questions you have about the risks with the study staff and/or your surgeon. You may or may not 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. Some other choices include surgery without the use of EXPAREL®, not participating in this study, or not undergoing surgery. Other options may be available such as alternative studies regarding pain management; you doctor can talk to you about these options if you are interested 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 Cynthia Emory, M.D., Principal Investigator. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is [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].

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 a soft tissue sarcoma that requires removal by undergoing surgery. 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 is to study a medication called liposomal bupivacaine (EXPAREL®). We want to see if it is safe and if it can reduce pain after surgery. We want to study its use after the removal a soft tissue tumor called a sarcoma.

EXPAREL® is a drug that has been approved by the US Food and Drug Administration (FDA). It has been approved for use for local pain relief around a surgical wound. It is not a narcotic medication. It is a non-opioid type of pain medication. However, it has not been approved for use yet in this condition. Its use in soft tissue sarcoma resection surgery is considered experimental.

Some surgeons use EXPAREL® as part of their standard clinical care. It is often used in other surgeries. We would like to study if the use of EXPAREL® in the removal of soft tissue sarcomas can help reduce pain after surgery. We also want to know if it reduces the amount of narcotic or opioid medications that patients take when they are in the hospital after surgery.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 20 people at Wake Forest Baptist Health will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

If you participate in this study, you will have surgery to remove your sarcoma. This is a part of your normal care. During your surgery, the surgeon will inject EXPAREL® into your leg around the surgery area. This is a part of research.

During your stay in the hospital after your surgery, a nurse will visit you at least 4 times per day (about once every 6 hours). This is standard of care and would happen regardless of whether or not you decided to be a part of this study. While you are in the hospital after your surgery you will have access to pain control medication as you normally would after a surgery of this type. Nurses will also record information on the amount of medications that you have used to control the pain and information on how long you stay in the hospital. If you leave the hospital before 4 days after surgery, we may contact you at home to collect this information.

We may take a photograph of your wound/surgical site. This is being done to document the size of the sarcoma resection. This is a part of normal care of the surgery and will be described to you in a separate surgical consent. However, we may use this photo to teach others how to inject EXPAREL®. We may use it for other teaching purposes. We may use it to describe how we injected EXPAREL® during this study. There will be no factors indicating your identity

included in the photograph. You can also withdraw your consent to use and disclose the photograph before it is used. You should also understand that you will not be able to inspect, review, or approve the photographs or other media (including articles containing such) before they are used for this study.

Please choose one of the following regarding the use and disclosure of the photograph used in this research study:

_____ I would like the photographs of me to be destroyed once their use in this study is finished.

____ The photographs of me can be kept for use in future studies provided they are kept secure and any future study will be reviewed by an IRB. I understand that I will not be able to inspect, review or approve their future use.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for 6 weeks after your soft tissue resection surgery.

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. If you decide to withdraw from the study, you will continue to receive the standard of care required for your condition.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. This research involves more than minimal risk to you. You should discuss the risk of being in this study with the study staff and your surgeon. Possible risks and side effects that may be related to the use of the medication EXPAREL® include nausea (upset stomach), constipation, vomiting (throwing up), allergic reactions, deep vein thrombosis (DVT: a blood clot a deep vein in your leg) and/or wound infection after surgery. A detailed list of side effects is listed below.

More Common (occurs in 10% or greater of patients)

- nausea,
- constipation,
- and vomiting

Less Common (occurs in 2-10% of patients)

- increased body temperature/fever,
- dizziness,
- increased fluid retention,
- decreased red blood cells,
- low blood pressure,
- itchy skin,
- increased heart rate,
- headache,

- difficulty sleeping,
- muscle spasms,
- low blood cell count due to a sudden loss of blood,
- back pain,
- drowsiness,
- procedural pain

Occurs in less than 2% of patients

- death
- chills,
- skin redness,
- Decreased heart rate,
- Inability to urinate,
- pain,
- swelling,
- tremor,
- dizziness when standing up
- Pins and needles or prickly feeling in the skin,
- fainting,
- incision site swelling,
- high blood pressure associated with the procedure,
- low blood pressure associated with the procedure,
- procedural nausea,
- muscular weakness,
- neck pain,
- itchy rash,
- Increased sweating,
- cold sweat,
- hives,
- abnormally slow heartbeat,
- racing heart
- irregular heartbeat,
- abnormally fast heartbeat,
- high blood pressure,
- pale appearance,
- anxiety (nervousness, fear, worry)
- confusion,
- depression,
- agitation,
- restlessness,
- low oxygen levels in your tissues,
- spasms of the vocal cords,
- temporary stoppage of breathing,

- respiratory depression, trouble breathing
- respiratory failure,
- body temperature increased,
- blood pressure increased,
- blood pressure decreased,
- oxygen saturation decreased,
- uncontrolled leaking of urine,
- blurred vision,
- ringing in the ears,
- drug hypersensitivity/allergic reactions

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.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. 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.

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. Possible benefits of participating in this study and the use of EXPAREL® may include but not limited to decreased pain after your surgery, a shorter stay in the hospital, and fewer medications needed to control pain after your surgery. There are no guarantees that you will experience any of these potential benefits.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. Instead of being in this study, you have the following options:

undergo the soft tissue sarcoma removal surgery without the use of EXPAREL®, undergo the surgery with the use of EXPAREL® but choose to not participate in the research study and data collection, or you can also decide to not have this soft tissue sarcoma removal surgery. You should talk to your doctor about all the choices you have.

WHAT ARE THE COSTS?

The medication, EXPAREL®, would be billed to your insurance in similar fashion as other local anesthetics used in the operating room or the cost of a peripheral nerve block. The cost of the medication is not provided by the study.

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.

Participant information may be provided to Federal and other 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.

During the surgery we may need to take a photograph of the surgical site. If this is necessary, there will be no factors indicating your identity included in the photograph.

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 the Department of Orthopaedic Surgery at Wake Forest Health Sciences. The researchers do not, however, hold a direct financial interest in the 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 Cynthia Emory, M.D. at [redacted] during normal business hours or after hours, call the after hours' pager. If calling the after hour's pager, dial [redacted] and then enter the pager id number [redacted] and press #. You will then enter your telephone number starting with the area code where you wish to be called back at and press # again. Your call should be promptly returned.

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**:**
patient name, medical record number, date of birth, date of surgery and information related to your surgery and treatment of the sarcoma.

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.

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 at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. 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 can tell Dr. Cynthia Emory 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:

Cynthia Emory, M.D.
[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.

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 North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH 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 it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

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 contact your surgeon, Cynthia Emory, M.D. at [redacted] during normal business hours or after hours, call the after hours' pager. If calling the after hour's pager, dial [redacted] and then enter the pager id number [redacted] and press #. You will then enter your telephone number starting with the area code where you wish to be called back at and press # again. Your call should be promptly returned.

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