Wake Forest™
School of Medicine

Department of Pediatrics

STUDY TITLE: A RANDOMIZED, DOUBLE BLIND TRIAL OF PEDIATRIC LUMBAR PUNCTURE UNDER SEDATION/TOTAL INTRAVENOUS ANESTHESIA (TIVA) WITH AND WITHOUT EMLA CREAM

Informed Consent Form to Participate in Research

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required and the assent (agreement) of your child may be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

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 are undergoing a lumbar puncture under general anesthesia. 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?

You are scheduled to have a lumbar puncture (LP or "spinal tap"). The purpose of this research study is to see if a skin numbing cream called EMLA (Eutectic Mixture of Local Anesthetic) cream will reduce the amount of total intravenous anesthesia (TIVA) (sleeping medicine) needed to effectively perform an LP. There are concerns among the anesthesia doctors and scientists about the effect of general anesthesia on patients' brains, especially children's brains. We would like to find ways to *reduce* the total amount of intravenous anesthesia administered to patients who require sedation for lumbar puncture, because giving less IV sleeping medicine is safer than giving more in most circumstances.

In this study Eutectic Mixture of a Local Anesthetic (EMLA cream) will be compared to placebo cream. 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 (EMLA cream) or placebo cream 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?

Approximately 40 people will take part in this study at a single institution: Wake Forest Baptist Medical Center in Winston-Salem, North Carolina.

WHAT IS INVOLVED IN THE STUDY?

If you agree to participate and sign the forms, at your study visit you will be randomized into one of the study groups described 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 placed in each group.
Neither you nor the investigator will know which cream (EMLA or placebo) 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.

If you decide to participate in the study, you will only be consented once. You may, however, undergo randomization as many times as you are having an LP done. That means you sometimes might get the placebo cream and sometimes might get EMLA cream. Each LP will require a separate randomization. You will not be asked to consent for the study at each clinic visit. You may stop participating at any time. You may also choose to participate in the randomization process for some LPs but not others. The choice is yours.

Treatment Group

If you are randomized into the treatment group, EMLA cream will be placed on your lower back and covered with a tape-like dressing when you arrive in clinic. You will then be seen in the hematology/oncology clinic as you normally are before going to the sedation suite for the lumbar puncture. Once in the sedation suite, the EMLA cream will be removed and your lower back will be cleaned in a sterile fashion. Next, you will be given IV medicines (usually propofol and fentanyl) to put you to sleep in order to effectively perform the lumbar puncture and administer intrathecal chemotherapy with little to no movement. The first doses of medicines are based on your weight, but additional doses may need to be given if you are moving too much during the LP. This is decided by the doctor performing the sedation, often together with the person doing the LP. During the time that you are asleep, your vital signs will be monitored and oxygen will be provided. Once the procedure has been performed you will be allowed to wake up on your own.

Placebo Group

If you are randomized into the placebo group, everything will be the same except placebo (fake) cream will be used instead of real EMLA cream. Placebo cream will be placed on your lower back and covered with a tape-like dressing when you arrive in clinic. You will then be seen in the hematology/oncology clinic as you normally are before going to the sedation suite for the lumbar puncture. Once in the sedation suite, the placebo cream will be removed and your lower back will be cleaned in a sterile fashion. Next, you will be given a dose of IV medicines (usually propofol and fentanyl) to put you to sleep in order

to effectively perform the lumbar puncture and administer intrathecal chemotherapy with

little to no movement. The first doses of medicines are based on your weight, but additional doses may need to be given if you are moving too much during the LP. This is decided by the doctor performing the sedation, often together with the person doing the LP. During the time that you are asleep, your vital signs will be monitored and oxygen will be provided. Once the procedure has been performed you will be allowed to wake up on your own.

For both groups, you will also be asked to complete a brief survey after each lumbar puncture to see if you/your parent(s) were satisfied with the sedation.

Your treatment for your disease or condition will not change. The schedule and doses of chemotherapy you receive (if applicable) will be the same whether you are on this study or not. You will be consented separately for the lumbar puncture to administer intrathecal chemotherapy. You will also be consented separately for the sedation that you will undergo as you normally would.

WHAT IS THE STANDARD OF CARE FOR LUMBAR PUNCTURES?

There is not a widely agreed standard of care for lumbar punctures (LPs). Some patients have LPs with no sedation and use local numbing medicine (injected into the skin). Some patients (including most children) require sedation for LPs. Some doctor's use EMLA cream and some do not. There has never been a study that shows that EMLA cream can reduce the amount of anesthesia medicine used for sedation.

How Long Will I Be in the Study?

You will be in the study for only as long as you wish. It could be as short as one day or as long as three years. One randomization and lumbar puncture occurs in one day. You may choose to have more LPs on study after the first one, or you may choose to stop being in the study after the first LP. Most patients with ALL receive about 20 LPs spaced out over 2.5 - 3 years. After that, you will no longer receive protocol therapy but you will still be in the study. Any research information collected from you in this study will be kept in the research records for at least six years after the study is finished.

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 EMLA cream are:

Common:

-Rash or Blanching of the skin

Rare:

-Methemoglobinemia - decreased ability of the blood to carry oxygen
-Anaphylaxis or Allergic reaction

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 amount of propofol given to each group will be monitored and recorded by the study team. This amount will be increased if there are signs that your child is not receiving adequate sedation. However, your child will never be given a dose that is outside the medical guidelines for safety of this drug.

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?

Based on experience with EMLA cream in other patients, researchers believe it may be of benefit to subjects undergoing lumbar puncture. It is possible that EMLA cream could allow less IV anesthesia medicine to be used to keep you still for the LP. Getting less IV medicine is probably safer than getting more. Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case. You are not expected to receive any other direct benefits from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, your options include:
1. You can choose to have your regularly scheduled lumbar punctures with or without EMLA cream while under sedation in the sedation suite.
2. You can choose to have the lumbar puncture performed without sedation, with or without EMLA cream on the lower back.

What About My Health Information?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:**
1. Total dose of propofol administered to you.
2. Blood pressure during the sedation
3. Amount of movement if any during the sedation.
4. Satisfaction with the sedation.

5. How long it takes you to wake up.
6. Anesthesia time and procedure time.

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. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his team, or others at Wake Forest Baptist Health who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest Baptist Health.

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 might no longer be protected by federal or state privacy rules.

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

You can tell Dr. Thomas McLean, MD that you want to take away your permission to use and share your Protected Health Information or research information at any time by sending a letter to this address:

Dr. Thomas McLean, MD
Department of Pediatrics
Medical Center Blvd
Winston-Salem, NC 27157

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 a special section of your medical record. This part of the medical

record will only be available to people involved in the research study or persons treating you at this Medical Center.

Information about this clinical trial will be placed in the clinical trial registry maintained by the National Institutes of Health/National Library of Medicine (NIH/NLM).

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.

This authorization is valid for six years or five years after the completion of the study, whichever is longer.

What Are the Costs?

There are no costs to you for taking part in this study. If you are randomized to receive EMLA cream, it will be billed to your insurance as it usually is. Insurance virtually always covers the cost of EMLA cream for children having invasive procedures. If you do not have insurance, please let your doctor know and EMLA cream will be provided free of charge. All other 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 YOU BE PAID FOR PARTICIPATING?

There are no plans to pay you for taking part in this study.

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.

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. Thomas McLean.

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, 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 about the study or in the event of a research-related injury, contact the study investigator

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.

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.

Signature of Subject/ Parent/Legal Guardian **Date:** **Time:** **am/pm**

Printed Name of Subject/ Parent/Legal Guardian

Name of Child in the study

Legal Guardian's Relationship to Child in study

Signature of Person Obtaining Consent **Date:** **Time:** **am/pm**