Locally applied antibiotics for infection prophylaxis in treatment of open fractures

NCT03705962

June 1, 2016

Informed Consent Form

IRB approved the June 1 2016 Version on June 10, 2016.

Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

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Charlottesville, VA 22908 Telephone: 434-243-0274

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a signed copy of this form.

This study will be funded by the Department of Orthopedic Surgery at University of Virginia

Why is this research being done?

An open fracture is an injury that occurs when a broken bone is exposed through the skin. This may mean that the bone is actually sticking out of the skin, or it may mean that the skin and soft-tissue is disrupted and exposes a path to the site of the fracture. Open fractures are a concern because these injuries can be difficult to heal, and infection can cause significant problems with the healing of the bone and the surrounding tissues. Most of the early treatment of an open fracture is focused on preventing the development or progression of infection at the site of the fracture.

The purpose of this study is to see if directly injecting tobramycin at the wound site at the time of your surgery to close the open fracture will decrease the risk of infection, as well as the risk of needing additional surgeries for infection after 6 weeks.

The standard of practice in treating open fractures is to administer antibiotics, such as tobramycin, intravenously (through a needle in a vein) until surgical closure of the open fracture and not as a localized injection. The surgical closure may occur any time within several days.

Tobramycin is approved by the Food and Drug Administration (FDA) for the treatment or prevention of infections that are proven or strongly suspected to be caused by bacteria. Tobramycin has been proven to be a safe and effective antibiotic in humans. It is most commonly used in an intravenous form (IV-through a needle in the vein) that is distributed throughout the body instead of a localized injection. This use as a local

injection has shown promise in an animal model and in preliminary clinical application. No randomized trial has been conducted at this time. **Therefore, the use of tobramycin in this study is considered to be investigational; it has not been proven to be safe or effective by the FDA when given as a local injection at the time of open wound fracture.**

If you agree to participate in this study, you will be randomized to receive tobramycin or placebo (saline injection. You will get this injection only once during this study, at the time of wound closure. However, if your doctor conducts another surgical procedure at the wound site, you will be given a second injection of the antibiotic tobramycin or placebo at the same wound site. The treatment of your injury will be the same whether you choose to be in the study or not. As part of your participation in this study, you will be followed for outcomes of infection rate, skin appearance and need for any further surgery for 6 weeks.

You are being asked to be in this study, because you have an open fracture, and are between 18 and 70 years of age.

Up to **133** people will sign the consent to be in this study at UVA.

How long will this study take?

Your participation in this study will require three (3) study visits over a six (6) week period of time. Each visit will last about 30 minutes for this study and will take place at the time of your scheduled surgery and follow up appointments.

What will happen if you are in the study?

SCREENING (will take about 30 minutes to complete):

Visit 1 ***(Day 1 of the study):***

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These assessments are done as part of your clinical care and the results will be recorded for research purposes. These include the following:

- Review of your medical history and medical records.
- Physical Exam
- Wound inspection
- X-rays of fractured limb
- If you are a female able to become pregnant, you will be asked if you are pregnant. Pregnant women are not permitted to take part in this study.

If these assessments show you are eligible, you will proceed with surgery and study procedures. If it is a medical emergency, you will be taken in for surgery immediately after signing the consent. If you are admitted to the ICU prior to surgery, the consent can be obtained any time prior to surgery.

RANDOMIZATION and STUDY PROCEDURES

You will be randomized (like the flip of a coin) before your surgery to one of two groups. You have an equal chance of being assigned to any one of the groups. Neither you nor your study doctor can choose which group you are assigned. Neither you nor your doctor will know which group you will get until the study is completed. But if your doctor needs to know, the people doing this study can find out.

GROUP 1: Study agent ***(antibiotic tobramycin) injected directly into the open fracture during surgery***

GROUP 2: Placebo (saline) ***injected directly into the open fracture during surgery***

Note: A placebo is a harmless substance that looks like the study drug, but which should have no effect.

Day of Surgery:

If you are in Group 1 (tobramycin), your doctor will inject the antibiotic at the site of your wound after closing your wound in the operating room. You will be getting an injection of the antibiotic at the wound site directly, in addition to the antibiotic you will be getting intravenously.
If you are in Group 2 (Placebo), your doctor will inject the placebo (saline) at the site of your wound after closing the wound.

FOLLOW UP:

- You will return to the hospital for standard follow up visits in Weeks 2 and 6. You do not make extra visits for the study. The number and frequency of follow-up visits for the study are part of standard of care
- During these visits, we will ask you how you are healing and about your medications, and perform your medical record review and take x-rays (part of standard care). All of these procedures will be the same in weeks 2 and 6. The information from the assessments will be collected and recorded for research purposes up to the 6 week visit.

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- You are required to come to clinic for each study visit.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks and side effects related to tobramycin:

You will be receiving local injection of tobramycin into your wound cavity (for research purposes) along with the standard treatment of intravenous injection of antibiotics by your doctor. Following are the risks you may have with receiving the local injection of tobramycin:

Less Likely

- Prolonged exposure to medicines similar to tobramycin have been associated with kidney dysfunction in people who do not have kidney disease. This drug effect is permanent and irreversible. The risk is greater in patients whose kidneys are not functioning well and in those who receive high doses of tobramycin for a long period of time.

- Numbness
- Skin tingling
- Muscle twitching
- Convulsions
- Dizziness
- Tinnitus
- Roaring in ears

Rare but serious

- Toxic to kidneys. This risk in greater in patients who already had kidney damage.
- Causes hearing loss and loss of balance. This drug effect is permanent and irreversible. This risk in greater in patients with preexisting kidney damage and in patients with normal kidney function, but treated with higher doses of tobramycin for longer periods of times than recommended

Kidney and nerve function will be closely monitored during surgery, especially in patients with known or suspected reduced kidney function at the onset of therapy, and also in patients who have normal kidney function, but develop signs that their kidney is not functioning efficiently during the study. This will be done through blood and urine tests. In high risk patients, audiograms will be done to see if there has been any signs of toxicity leading to hearing loss and loss of balance.

Concurrent use of other drugs like amikacin, streptomycin, neomycin, kanamycin, Tobramycin, paromycin, cephaloridine, viomycin, polymyzin B, colistin, cisplastin, and vancomycin should be avoided. Other factors that may increase patient risk are dehydration and advanced age.

Risks from Placebo: There is the risk that you will not receive the additional study drug. However, you will receive systemic antibiotics in your IV both before and after surgery as the standard care for open fractures.

Risks from Completing Questionnaires:
Some of the questions asked may make you angry, emotionally upset or stressed out not or at a later time. If this occurs, you can contact the following person for help ***(your doctor Seth Yarboro MD at*** (434) 243-0274***).*** If you do not wish to answer a question, you may skip it and to the next question

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You may or may not benefit from being in this study. If you are randomized to receive the tobramycin possible benefits include: decreased risk of infection at the wound site, decreased risk of need for re-operation, increased bone healing
In addition, information researchers get from this study may help others in the future. If the results from this study are positive and prove to help people with open fractures heal better, faster, and with less pain, the injection of local antibiotics could become the standard of care for people in the future who suffer injuries involving open fractures.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- Systemic IV antibiotic Cefazolin before and after surgery, as well as any other antibiotics based on your injury.
- Tobramycin given locally into the fracture wound at the time of wound closure.

If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will not get any money for being in this study.

Will being in this study cost you any money?

For the purpose of this study, the cost of the single local injection of either tobramycin or placebo will be provided free of charge to you and/or your insurance company. You and/or your insurance company must pay

for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and they require you to get their permission before you decide to be in the study.

You will be responsible for the cost of travel to come to any clinic visit and for any parking costs, and these will be required for standard care of your injury, regardless of participation in the study.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your fracture
b) Your condition gets worse
c) The side effects of receiving a local injection of tobramycin are too dangerous for you
d) New information shows the local injection of tobramycin will not work or is not safe for you

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:

Seth Yarboro, MD
University of Virginia
Orthopaedic Surgery, School of Medicine
Box 800159, HSC
Charlottesville, VA 22908 Telephone: (434)243-0274

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483

Charlottesville, Virginia 22908 Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

If an interpreter is involved in the consent process because the potential subject does not speak English well or at all, the participant should NOT sign on the line above – leave this line blank. Instead, the participant should sign the Short Form or full consent written in the language they can understand.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study has been fully explained to the potential subject in a language they understand and have answered all their questions.

_____	_____	_____
INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this study to a potential subject, the interpreter must sign and date the line above.

Surrogate Consent

In the event the adult participant is unable to give informed consent for participation in this study:

_____/_____ _____

PERSON GIVING CONSENT FOR PARTICIPANT (Signature/ Printed) DATE

RELATIONSHIP TO PARTICIPANT: _____

If an interpreter is involved in the consent process because the surrogate does not speak English well or at all, the surrogate should NOT sign on the line above – leave this line blank. Instead, the surrogate should sign the Short Form written in the language they can understand.

Person Obtaining Consent of the Surrogate

By signing below you confirm that you have fully explained this study to the potential subject's surrogate, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Attending Physician Approval

I am the doctor that provides medical care for this subject. I believe that his/her health might be helped by being in this study. I approve his/her participation in this research study.

_____	_____	_____
ATTENDING PHYSICIAN (SIGNATURE)	ATTENDING PHYSICIAN (PRINT NAME)	DATE

Note: If the researcher is also the attending physician for the patient, they may also sign here as the attending physician.

Person Obtaining Assent of the Adult Subject

The subject is unable to give assent due to the following reason:

_____

OR

By signing below you confirm that the study has been explained to the adult subject, all questions have been answered and the adult subject has not demonstrated resistance or dissent by word or gesture to enroll in the study. You also confirm that if the subject demonstrates resistance or dissent at any point in the study that they will not be subjected to any additional study interventions.

PERSON OBTAINING ASSENT (SIGNATURE)	PERSON OBTAINING ASSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study has been fully explained to the potential subject's surrogate in a language they understand and have answered all their questions.

INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this study the interpreter must sign and date the line above.

Consent of the Participant to Continue to Be in the Study

Your legal representative gave his/her permission for you to be in this research study. This is because you were not able to make your own decision due to your illness. Your condition is now better. You are being asked to decide whether to continue to be in this study. The decision is up to you. Before you sign this form, please ask questions about any part of this study that is not clear to you. When you sign below, you are saying you understand the information we gave you about the study and in this form.

If you sign this form it means that you agree to continue being in the study.

PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

If an interpreter is involved in the consent process because the subject does not speak English well or at all, the subject should NOT sign on the line above – leave this line blank. Instead, the subject should sign the Short Form written in the language they can understand.

Person Obtaining Consent of the Subject

By signing below you confirm that you have fully explained this study to the subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Interpreter

By signing below you confirm that the study has been fully explained to the potential subject in a language they understand and have answered all their questions.

INTERPRETER (SIGNATURE)	INTERPRETER (PRINT)	DATE

If an interpreter was used to explain this study to a potential subject, the interpreter must sign and date the line above.

Consent from Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject
☐ Subject's surrogate

IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE