

A Phase I/II Double-Blinded Randomized Prospective Study standard of Sterile Amniotic Fluid Filtrate Epidural Injection for the treatment of Lumbosacral Radicular Pain due to Spinal Stenosis: Improving Safety and Outcomes in the Treatment of Pain and Disability Related to Spinal Stenosis.

Principal Investigator: Zachary McCormick, MD
ICF Version 7 (13AUG2024)

Page 1 of 10

Consent and Authorization Document

BACKGROUND

You are being asked to take part in a research study. Before you decide, you need to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with friends and relatives if you wish. Talk to the research doctor or staff if anything is unclear or if you need more information. This is a volunteer research study.

The purpose of this research study is to observe the outcomes of epidural injections of Human Amniotic Fluid (hAF) compared to the corticosteroid dexamethasone to determine which is more effective for the treatment of your low back pain diagnosis of lumbosacral radicular pain due to spinal stenosis.

Corticosteroid dexamethasone injections are a standard of care procedure; the hAF epidural injection is a new biologic treatment that is investigational and has not yet been approved by the FDA. Human Amniotic Fluid has been approved by the FDA for use in this research study.

You and your physician have decided on performing one of these procedures for your chronic lumbosacral radicular pain. These two procedures have never been compared in an appropriately designed head-to-head study. As such, the goal of the study is to determine if individuals with lumbosacral radicular pain who are treated with hAF epidural injection compared to corticosteroid dexamethasone epidural injection have a greater likelihood of experiencing meaningful relief of low back pain symptoms, functional improvement, and reduction of analgesic medication use at both short and long-term follow-up. This will be a randomized study, meaning you be randomly placed in the hAF or the corticosteroid group. You and your doctor will not choose which group you are placed in.

The investigator(s) of this research study would like to accomplish this study by evaluating a set of standardized questions and looking to see how the use of analgesic medication may or may not have been reduced.

STUDY PROCEDURES

If you agree to participate in this study, and you are 18 years or older you will be asked to sign this consent form. If you are pregnant or plan to become pregnant you will not be eligible for this study. Your participation in this study will involve collecting your medical history, demographics (age, sex, BMI) duration of back pain, nature of pain (i.e., bilateral, symmetrical, unilateral), exact anatomic location of lumbar pain based on clinical diagnosis aided by radiologic information. In addition, you will be asked to describe your pain level, changes in activity limitations, symptoms, emotions and overall quality of life related to your painful condition and to list or give a record of the opioid and non-opioid analgesic use up to 2 weeks before your scheduled procedure in the form of a survey questionnaire. It is estimated it will take approximately 10-15 minutes



Procedure Visit:

Today for the treatment of your low back pain you will be receiving one of the two procedures described below:

1. Group #1: Transforaminal Epidural human Amniotic Fluid (hAF) Injection Procedure
2. Group #2: Transforaminal Epidural Corticosteroid Dexamethasone Injection Procedure

If you are a woman of childbearing potential, a urine pregnancy test will be completed before any of the study injections.

During the injection procedure, you will be positioned prone (on your stomach/face down) on a fluoroscopy table. Blood pressure and pulse oximetry monitors will be placed. A pre-procedure time-out will be performed, as is protocol in this spine practice. Once in position for the injection procedure, you will be randomized to either group #1 or #2 based on a random computer-generated schedule. You will be blinded to the group to which you are randomized. The physician performing the injection will also be blinded to the group. Research personnel will prepare the medication to be used such that the physician cannot distinguish between groups. Identical syringes will be used in both groups and the syringe will be covered by a sticker making them indistinguishable in a syringe.

Each injection includes the following process. Using x-ray guidance, a lumbosacral epidural injection will be performed. An x-ray-guided injection procedure includes exposure to a small amount of radiation, similar to a plane flight across the United States. 2-5cc of 1% lidocaine will be injected into the skin and subcutaneous tissue to numb the area over the site of planned entry. A small needle will be used to access the epidural space. The needle tip position will be confirmed by x-ray guidance as well as with injection of a standard 1-3mL of contrast material visualized by x-ray, the current practice standard. Then, depending on the previously assigned randomization, 3 mL of amniotic fluid (hAF) or 1 mL of dexamethasone sodium phosphate combined with 2 mL of sterile water will be injected through the spinal needle.

Unilateral “one-sided” injections will be offered if your symptoms are present on only the left side or only the right side, while bilateral “two-sided” injections will be offered if your symptoms are present on both the left and the right and if your physician determines that this is medically appropriate. For multi-level symptoms, the treating physician will choose the one level with most prominent symptoms. Following injection, the needle will be removed from the entry point. A band-aid will be placed and you will be transferred to the recovery room. Approximately 15 minutes after the procedure, you will be discharged from the clinic with written discharge instructions (current standard practice). A post-procedure pain score will be collected.

If you choose to take part in this study, you are being asked to participate in a randomization of these two standard-of-care procedures using a computerized generated 1:1 method randomization. This means you have a 50% chance of being assigned to either group. It is anticipated that each group will have 56 participants.

Procedure Visit continued:

Following the Standard Treatment Procedure visit, routine scheduled follow-up will occur within 12 hours, after 48 hours (+/- 5 hours), 3 weeks (+/- 7 days), 6 weeks (+/- 14 days), 3 months (+/- 20 days), 6 months (+/- 20 days), 12 months (+/- 30 days) and 24 months (+/- 30 days), at which times all follow-up measures will be obtained. At each window, a minimum of 10 attempts will be made to reach you to collect outcomes. You will have the option to complete surveys via a postage-paid reply mail survey, telephone interview, or a web-enabled survey which can be completed by phone or computer. Data collection will be performed using a web-enabled content management system that is a password-protected system hosted on a HIPAA-compliant server that is routinely backed up, to help ensure your information is protected. Again, you will be asked to answer questions about your pain level, changes in activity limitations, symptoms, emotions and overall quality of life related to your painful condition and to record your current use of opioid and non-opioid analgesics. This part of the survey should take 10 minutes.

For ease of completion of follow-up questionnaires, you will have the option to complete the questionnaires using a free mobile device app, available from our data collection vendor, STATIX L.L.C. Key features of the app include push notifications to remind you when it is time to complete a survey and functions to edit contact information and preferences. The mobile app is available as an option for completing the questionnaires. You will also have the option to complete the questionnaires through email, telephone interviews, and postage-paid mailed paper questionnaires if that is your preference.

If you decide to use the mobile device app, reminders will be sent to you when it is time to complete a follow-up questionnaire. Once you complete the questionnaire in the app, no additional follow-up reminders will be sent until it is time for you to complete the next one. Your answers will be uploaded to STATIX's secure data collection site. If you make changes to contact information, preferences, and PRO survey answers through the app, these changes will be reflected in the data collection site.

The mobile app is available for free on both IOS and Android platforms, available from the following sites, which contain screenshots and the app privacy statement.

Apple App Store: <https://apps.apple.com/us/app/statix/id1604450099>

Google Play Store: <https://play.google.com/store/apps/details?id=com.statix>

If you decide to use the mobile app, you will be required to log into it using the same credentials (email and password) as you will create for the web-based surveys. If you are using the website or mobile app, you will be asked to create a password at the time that you are first enrolled into the study.

The mobile app will enable push notifications to your device to remind you when a survey is due to be completed. As with any app, you can disable notifications within your device. The mobile app will not collect your user history, device information, location tracking, or other data elements other than the survey data obtained through the app as part of the research you are agreeing to participate in.

Procedure Visit continued:

You may be requested to have a laboratory blood draw ~ 4 weeks after your initial injection. There are risks associated with this blood test which are disclosed below.

The study start date and the outcome assessment timeline will begin at the date of your initial procedure/treatment. You may request an additional treatment within the first 3 months of this study if you are not experiencing adequate pain relief. This will be a decision made by you and your physician. After 3 months from the initial injection, if you wish to receive the alternative treatment, you may cross-over to the other group. As part of the crossover group, you would once again follow up with your physician within the first three months to discuss pain relief. If you have not received adequate pain relief an additional treatment may be discussed as well.

This study is intended to monitor outcomes for 2 years following the epidural injection procedure.

Crossover: At the 3-month follow-up, any participant who has not obtained adequate pain relief can request to cross over to the alternative treatment group. For safety, you'll be contacted again at 12 and 48 hours after the injection. You'll resume the study schedule starting at Visit 6.

RISKS

The risks associated with using Amniotic Fluid (hAF) as a treatment for radicular back pain are unknown.

You may be requested to have a blood test. A human leukocyte (HLA) test is performed to see if a person is having an immune response to the study drug injection. You may have discomfort, possible bruising, and redness around the site of the blood draw, as well as the feeling of lightheadedness.

These procedures will expose you to radiation. The risk from this radiation exposure is considered to be small and comparable to other everyday risks. To give you an idea of how much radiation you will receive, we will compare this radiation to the radiation that you receive from natural sources. Everyone receives a small amount of unavoidable radiation every day. Some of this radiation comes from space while some comes from radiation that is naturally occurring in water, soil, rocks and minerals found in plants and animals. The excess radiation that you will be exposed to in this research study is equivalent to about 6 months of natural background radiation. This amount does not include any radiation exposures that you may receive from other types of tests.

RISKS continued

You may also experience the following symptoms as a result of the Epidural Injection of Amniotic Fluid (hAF) or Corticosteroid:

Temporary/short-term pain or discomfort around the area treated

Temporary muscle soreness/muscle spasm

Infection

Minor bleeding

Allergies or reactions to medications used (specifically: human Amniotic Fluid, Iohexal, lidocaine, or dexamethasone phosphate)

Nausea

Exacerbation of typical back and/or leg pain

Insomnia

Heart palpitations

Anxiety

Facial Flushing

Randomization

Your doctor will not make the decision which procedure you will have, there may be risks associated with one procedure that are not associated with the other.

Surveys/Questionnaire

There may be some discomfort or emotional distress at describing your current health circumstances as you fill out the questionnaire or discuss with your health with a study team member. In addition, there is a very rare yet remote possibility there could be a loss of confidentiality (e.g. inadvertent disclosure of study data and or personal health information).

UNFORESEEABLE RISKS

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

BENEFITS

There may be no additional health benefits to you for being in this study. We hope that the information obtained from conducting this study will help us provide more accurate therapeutic standards for patients like you who have chronic low back pain and by so doing we can improve patient care in the future.

ALTERNATIVE PROCEDURES

If you choose not to be in this study, a number of treatment choices may be open to you. Please discuss this with your healthcare provider. Some of these may include, relief from conservative treatment options including physical therapy, non-steroidal anti-inflammatory drugs (NSAIDS) and other treatment options.



PERSONS TO CONTACT

If you have questions, complaints or concerns about this study, you can contact Dr. Zachary McCormick on the research line at (801) 587-1493 or contact Dr. McCormick's assistant at (801) 213-6980. If this is after hours, please contact the hospital operator at (801) 581-2121 and ask for the Physical Medicine and Rehabilitation resident on call.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY

If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs of such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for the medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.

The University of Utah is a part of the government. If you are injured in this study and want to sue the University or the doctors, nurses, students or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

It is your choice to be in the study. You can change your mind and stop being in the study at any time, and it will in no way affect the health care you would normally get. Your participation in this study is completely voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.



RIGHT OF INVESTIGATOR TO WITHDRAW PARTICIPANTS

Your study doctor may decide to remove you from this research study without asking you if at any time he or she feels that the research study is not in your best interest. Some, but not all, of the reasons you may be removed from this research, may be that you have not followed the instructions of your study doctor.

COSTS AND COMPENSATION TO PARTICIPANTS

Costs related to standard-of-care will be charged to your insurance company. Your initial office visit with your doctor and follow-up appointment are considered standard of care. The epidural injection procedure and medication will be covered by the study and provided to you free of cost. The epidural injection procedure will require fluoroscopic guidance. Up to four of the fluoroscopic guided injection procedures you will receive are considered a part of your standard care and you will receive them regardless of your participation in this study. Up to two of the fluoroscopic guided injection procedures are research related and you are only receiving them because you chose to be enrolled in this research study.

If you have concerns regarding costs or billing, you will want to discuss your coverage and responsibilities with your health insurance company. Procedure authorizations are done through the University of Utah scheduling team. For questions regarding authorization status, you may contact them. There will be no costs to you for participating in the research portion of this study.

For your time, you will receive a \$50.00 stipend after you complete all surveys and questions leading up to and including the 6-week follow-up survey questionnaires (this includes questionnaires before the procedure and 3-week follow-up). You'll receive another \$50.00 stipend after you have completed all surveys and questions leading up to and including the 12-month follow-up survey questionnaires (questionnaires for the 3-month, 6-month, and 12-month follow-up). You'll receive a final \$50.00 stipend after you have completed the final survey/questions at the 24-month mark of this study. If all of the study questionnaires have been completed, you will receive a total of \$150.00.

If you choose to crossover at the 3-month time point, you will have another 12 and 48-hour phone call for safety. After that, you'll resume the study schedule starting at Visit 6. The compensation amount stays the same.

Study Visit Schedule								
Baseline Visit	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
In Clinic	12-hour Phone Call	48-hour Phone Call	3-Week Survey	6-Week Survey	3-Month Survey	6-Month Survey	12-Month Survey	24-Month Survey
\$50.00					\$50.00			\$50.00

NEW INFORMATION

Sometimes during a research project, new information or treatments may become available about the subject of chronic lower back pain. If this happens, your research doctor will tell you about it and discuss with you whether you would like to continue in the study.

NUMBER OF PARTICIPANTS

We expect to enroll a total of 112 participants at the University of Utah.CONFLICT OF FINANCIAL INTEREST

The University of Utah has a significant institutional financial interest in intellectual property being used in this study (U-5650 "Amnion/Chorion Membrane as a Wound Cover to Control Adhesions and Heal Wounds, Amniotic Fluid (Supernatant) and Amniotic Fluid (Whole) to Reduce Inflammation, Heal Wounds and Stimulate Bone Growth") and a significant institutional financial interest in Eliksa (a non-publicly traded company which is licensing the technology for commercialization). This is a conflict of interest as determined by the University of Utah Institutional Conflict of Interest Officer and a management plan has been implemented to ensure transparency, promote data integrity, and to safeguard human participants in the research.

Investigator Jan Pierce has a financial interest in Eliksa, (a non-publicly traded company that is licensing the technology for commercialization), which is a conflict of interest as determined by the University of Utah Individual Conflict of Interest Committee, and a management plan has been implemented to ensure transparency, promote data integrity, and to safeguard human participants in the research.

In studies like this where there is a conflict of interest, an organization (called the Conflict of Interest Office) will create and manage a plan to ensure that the data from this study is accurately reported and correctly interpreted. This helps to make certain that the study is conducted correctly, and that participants in the study are treated in the fairest way possible.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records: Demographics and identifying information like name, address, telephone number, email address, age sex, date of birth, BMI. Related medical information about you like your personal medical history, allergies, current and past medications or therapies, and information from physical examinations, such as blood pressure reading, heart rate, temperature, procedure results, and radiographic images.

How will my information be protected and shared?

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password-protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and healthcare operations of the hospital. The sponsor, sponsor representatives, persons or companies contracted by the sponsor may see your PHI. We may also need to disclose information if required by law.
- 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 website at any time.
- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
 - Members of the research team.
 - The University of Utah Institutional Review Board (IRB), which reviews research involving people to make sure the study protects your rights;
 - the U.S. Food and Drug Administration (FDA)
 - DSMB Board Members and Data Coordinating Center
 - Other regulatory agencies
- If we share your identifying information with groups outside of the University of Utah Health, the groups may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.
- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive healthcare services at the University of Utah.

What if I decide to Not Participate after I sign the Consent and Authorization Form?

You can tell us at any time that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

CONSENT and AUTHORIZATION

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I understand that I will be given a signed copy of the consent and authorization form to keep.

I agree to take part in this research study and authorize study personnel to use and disclose health information about me for this study as has been explained in this document.

I understand that at any time, I can tell the study staff that I do not want to be in this study and do not want my health information to be used. I can also submit the changes to the study staff in writing. If I change my mind, the study team will not be able to collect new information about me, and I will be withdrawn from the research study.

However, I also understand that the sponsor can continue to use the information the study team has already started to use in the research as needed to maintain the integrity of the research.

By signing this consent form, I have not waived any of my rights which I otherwise would have as a participant in a research study.

I understand that this consent and authorization form has no expiration date.

Participant's Name

Participant's Signature

Date

Name of Person Obtaining
Authorization and Consent

Signature of Person Obtaining
Authorization and Consent

Date

