Cover Page for ClinicalTrials.gov

Document:
Informed Consent Form

Brief Title:
Localized Injection of Lidocaine and Glucocorticoid for Headache Treatment Phase 1 (LIGHT 1)

Official Title:
Intra-Arterial Injection of Lidocaine and Glucocorticoid in the Treatment of Intractable Headaches: A Non-Randomized, Open-Label Phase 1 Clinical Trial

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Cooper University Hospital

INFORMED CONSENT AND HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) AUTHORIZATION FORM

Title of study: Intra-Arterial Injection of Lidocaine and Glucocorticoid in the Treatment of Intractable Headaches: A Non-Randomized, Open-Label Phase 1 Clinical Trial

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Study Sponsor: Department of Neurosurgery, Cooper University Health Care

Study Funding: Grant Support from Society of Vascular and Interventional Neurology

Subject Name: _____

What does informed consent for a research study involve?

- The investigator or their staff will explain this research study to you.
- Participation is voluntary. This means you choose whether or not you want to take part in this research study.
- You do not have to take part in this study to receive treatment at Cooper.
- You can agree to take part, and then later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want.
- You will receive a copy of this form to keep.

Summary:

You are being invited to take part in a research study for a new treatment for chronic headaches (also known as “intractable migraines”) that have not been treated with other treatments. The purpose of this study is to see how safe this new treatment is, and how well this new treatment may work for your headaches. The treatment is experimental. It involves using very small tubes, called catheters, placed into one of the blood vessels in either your wrist or hip/groin. Two drugs, lidocaine and methylprednisolone, will be injected. Continuous X-rays (fluoroscopy) will be used to see where the catheter is in your body during the injection. You will receive these injections only one time. You will also be asked questions about your past medical history, medications, asked to do a few physical tests, and fill out a few surveys about your headaches over the course of a total of about 4 months.

You may or may not have benefit from this treatment. There is a possibility that your headaches worsen. There are risks or discomforts associated with this treatment, including infection, bleeding, or swelling

at the wrist or hip/groin where the needle is inserted, headache, dizziness, nausea, or allergic reaction. Your participation at any point of the study is voluntary.

Introduction:

You are being invited to take part in a research study (also called a clinical trial). This is a phase 1 clinical trial, and the treatment is experimental. This research will study drugs known as lidocaine (Xylocaine®-MPF) and methylprednisolone (SOLU-MEDROL®). It is your choice if you want to be in this study or not.

Research studies are different from regular care. Research studies are ways of finding out new information that might help other people with similar conditions or illnesses to yours. This form explains why we are doing the study, and how the treatment that is being offered to you is different from regular care. It tells you what will happen during the study. It also tells you about any inconvenience, discomfort or risk with this study. It also gives you a complete description of the treatment offered. This information will help you decide whether you wish to be part of the study.

What is the purpose of this research study?

Chronic headaches are a problem that negatively affects quality of life. New approaches to treating these headaches are of interest, especially in patients that have not had good relief after using other available treatments. Lidocaine is a commonly-used local anesthetic drug, which means that this medication works by blocking pain signals. Methylprednisolone is a steroid drug that reduces inflammation and swelling. Prior studies have shown that these medications, when injected into certain blood vessels in the brain, seem to give people some relief from their headaches. But this treatment has only been given in a very small number of patients before.

In our study, we hope to better learn how injecting both of these medications in low doses into two arteries in the brain may be a safe way to help improve the pain from chronic headaches. The treatment with this combination of two medications (lidocaine and methylprednisolone) is experimental and investigational.

The word “investigational” means the study drug is not approved by the U.S. Food and Drug Administration (FDA) to be used in this way, and is still being tested in research studies. In this study, the combination of giving the following two medications through the middle meningeal artery, an artery in your brain, is investigational:

- Xylocaine®-MPF (lidocaine hydrochloride)
  Manufacturer: Fresenius Kabi, LLC) and
- SOLU-MEDROL® (methylprednisolone sodium succinate)
  Manufacturer: Pharmacia & Upjohn Co, Division of Pfizer Inc).

This research study will involve you meeting with your study doctor to review your health history and answer a few questionnaires about your headaches. You will be asked to get blood work to check your salt and sugar levels. To receive the injections of the two study medications, you may receive sedation with monitored anesthetic care (MAC) (also known as “twilight anesthesia”). A doctor will position a small tube, called a catheter, into your blood vessel. The tube is very small, and the tube’s width similar to a skinny piece of spaghetti pasta. Starting from a vessel either in your wrist or in your hip/groin, the

doctor will steer this tube through the other connected blood vessels in your body until it reaches a blood vessel in your brain, called the middle meningeal artery. Through this small tube, both medications - lidocaine and methylprednisolone - will be injected. The tube will be removed. This entire procedure will happen under fluoroscopy, which is a continuous X-ray image that helps the doctor see where the tube is located in the body throughout the entire course of the procedure. The amount of radiation exposure from this is similar to the amount of natural background radiation over a 2 year time-period. For four weeks before and for three months after the injection, you also will maintain a log of your headaches using a diary provided to you by the study team, and meet with your doctor to discuss your symptoms and answer questionnaires about your headaches.

Who may or may not take part in this study?

To take part in this study, you must have the diagnosis of chronic headaches after having tried four types of treatment without success. This is also known as having an "intractable migraine." To qualify as having tried a treatment, this includes either needing to stop a treatment early due to side effects or trying a treatment without your symptoms getting better. You also need to be an adult (18 years or older in age), and need to be a current patient under the care of a Cooper University Health Care doctor for these headaches.

The study doctor or study staff has discussed with you the requirements for being in this study. It is important that you are completely honest with the doctor and staff about your health history. You should not take part in this study if you do not meet all requirements.

You cannot participate in this study if:

- You are pregnant and/or breastfeeding, or are not willing to practice birth control during the study.
- You have an active infection or other serious condition, like brain cancer.
- You have another medical condition of the brain, such as a brain tumor.
- You have a medical reason ("contraindication") that would make getting continuous X-ray imaging (fluoroscopic angiography) very risky.
- You have a medical reason ("contraindication") or other hypersensitivity that would make it risky to receiving either lidocaine or methylprednisolone drugs, which includes:
    - You have a prior history of reactions to local anesthetics
    - You have a systemic fungal infection
    - You have a severe allergy to cow's milk or other dairy products.
- You have a history of issues with anesthesia or local anesthetic medications, including conscious sedation/monitored anesthesia care (MAC) (also known as "twilight anesthesia").
- You are participating in another research study with an experimental treatment.
- You are taking certain medications that may interact with lidocaine or methylprednisolone. Your doctor will go over this comprehensive list.
- Your blood sugar level is too high (>400 mg/dL).
- You have another condition that the physician determines would make your participation in this study a risk to your safety.

How long will the study take and how many people will take part?

Your participation in this study will last approximately 4 months. The entire study is expected to take about 1 year to complete. We expect 20 people at Cooper will be in the study.

What will you be asked to do if you take part in this study?

You will be asked to visit your doctor or staff member in the office after enrollment, 1 week after treatment, 6 weeks after treatment, and 12 weeks after treatment. You will be asked questions about your medical history and medications you take. Your vital signs, including heart rate and blood pressure, will be measured. The doctor or staff member will ask you to do a series of simple physical tests to assess your nervous system. You will be asked to fill out three surveys regarding your migraine symptoms. In between study visits, you will be asked to maintain a journal of your headache symptoms and any changes in your medical history and medications. You will start this journal at the first visit, and you will continue logging your symptoms until 12 weeks after your treatment.

Only at the first visit, you will be asked to take a pregnancy test (if you are of child-bearing age). At the first visit and on the day of treatment, about 1 teaspoon (4.5 mL) of blood will also be drawn for a comprehensive metabolic panel to check your sugar levels.

To receive the treatment, you will be scheduled within four weeks of your first visits. You will come to the neurointerventional suite at Cooper University Health Care. You may receive monitored anesthesia care (MAC) (also known as "twilight anesthesia"), which involves giving you some anesthesia medications to numb any pain but does not require a breathing tube. A needle will be used to enter an artery in either your wrist or your groin/hip. We will use very small tubes, called catheters, to reach the middle meningeal arteries in your brain under imaging guidance. We will inject 40mg of lidocaine (2 mL or about 1/2 (half) of a teaspoon), followed by 20mg methylprednisolone (0.5mL or about 1/10 (one-tenth) of a teaspoons), into both of your middle meningeal arteries, which are blood vessels in your brain. We will then apply a seal to your wrist or groin/hip to help the area heal.

Please see the below table as a summary of what will happen at every visit:

	Visit 1 (Screening)	**Visit 2** (Treatment, Within 4 Weeks)	**Visit 3** (1-week Follow-Up)	**Visit 4** (6-week Follow-Up)	**Visit 5** (12-week Follow-Up)
Informed Consent Form	X				
Medical History Review and Medications	X	X	X	X	X
Physical Tests	X	X	X	X	X
3 Headache Surveys	X	X	X	X	X
Vital Signs (Heart Rate, Blood Pressure, etc.)	X	X	X	X	X
Blood Work	X	X			
Pregnancy Test	X				

Headache Journal	X	X	X	X	X
Treatment		X			

What are your alternatives (other choices) if you do not take part in this study?
The alternative is to not take part in this research study. This may include continuing your current care, such as continuing your current medications for chronic headaches. You may also try other medications that may be available for this condition, such as other antiepileptic drugs, beta-blockers, antidepressants, angiotensin receptor blockers and angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory agents (NSAIDS), ergots, triptans, analgesics (i.e., acetaminophen), botulinum toxin injections, or calcitonin gene-related peptide monoclonal antibodies. You may discuss these options with the study doctor or a doctor not associated with the study.

What are the possible risks or discomforts if you take part in this study?
Possible risks or discomforts if you take part in this study include:

- Exposure to radiation during the imaging procedure
- Allergy to the contrast agents
- Slight burning at the site of contrast injection during imaging procedure
- Small risk of bruising, infection, bleeding, injury to the vessels, or swelling at site where needle is inserted (either wrist or groin/hip) for giving the treatment
- Risks that are associated with the study drugs, including rarely: methemoglobinemia (blood disorder that affects your ability to get oxygen to your organs), familial malignant hyperthermia (a severe reaction to anesthetic drugs), confusion, convulsion, allergic reaction, increasing your risk of infection (including fungal infections), high blood pressure, increase in the amount potassium and calcium are filtered by your kidneys, a neurological event (such as stroke or paralysis), large change in your sugar levels, rupture of a small part of the heart after a recent heart attack, and issues with your heart rate or breathing.
- Pain during treatment or after treatment
- Dizziness
- Nausea and/or Vomiting
- Temporary discomfort when a blood sample is taken. There are no major risks of having blood drawn. It may be uncomfortable and can sometimes cause a bruise. In rare cases, it can cause fainting. Only trained people will draw your blood.
- Excessive or prolonged sedation from the sedative medications used for twilight anesthesia/MAC. This may potentially require placing a breathing tube (intubation).

During the study visits with your doctor, we may ask you some questions that seem sensitive or personal, such as drug use, alcohol consumption, and medical history. You can skip any question you do not want to answer.

There may be risks from the experimental procedures or investigational products that are currently unknown.

The data that we collect for this study will include personal information that could identify you, such as your name. Your privacy is very important to us. We have taken necessary precautions to keep your data

safe and confidential. There is a small chance that we could accidentally disclose this information to others. Details on how we will protect your information are described in the Confidentiality section of this form.

Can you take other medications while you are in this study?

You must inform your study doctor of any medications that you are taking. This includes:

- Prescription medicines other doctors have given you
- Over-the-counter medicines
- Herbal and "natural" products
- Vitamins and food supplements
- Any other special products you are taking.

During the study, do not start taking any medicines without talking to the study doctor first.

The following medications may not be able to be taken long-term while in this study. Please let your doctor know if you are taking any of the following medications on a regular basis that may interact with lidocaine or methylprednisolone. Your doctor will review the risks associated with them, and determine whether it would prevent you from safely participating in this study: nitrates/nitrites, local anesthetics, antineoplastic agents, antibiotics, antimalarials, anticonvulsants, acetaminophen, metoclopramide, quinine, sulfasalazine, amphotericin B, diuretics, aminoglutethimide, macrolide antibiotics, anticholinesterases, antitubercular drugs, cholestyramine, cyclosporine, digitalis glycosides, estrogens (including oral contraceptives), hepatic enzyme inducers/inhibitors, and ketoconazole.

What if you are pregnant or become pregnant?

Being a part of this study while pregnant might cause harm to your unborn child that we cannot predict. Therefore, we will not include pregnant women in the study. If you are a woman who may become pregnant, we will ask you to complete a pregnancy test and will not enroll you unless the test results are negative.

If you are sexually active, you must agree to use medically acceptable contraceptive measures for the duration of the study. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). If you are not willing to use one of these acceptable methods of birth control, we ask that you do not participate in this study.

If you do become pregnant during this study, you must inform the study doctor immediately.

Please inform your partner that if pregnancy occurs, you will need to report it to the study doctor, and they should promptly notify their doctor of your participation in this study.

Will there be any benefits if you take part in this study?

You may or may not receive any benefit from participating in the study. It is possible that you may get better, stay the same, or get worse. Other people with chronic headaches may be helped in the future based on what we learn from this study.

Will you be paid to take part in this study?
You will not be paid to take part in this study.

Will there be any costs to you to take part in this study?
You will not have to pay money to participate in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further.

What will happen to your blood samples collected as part of this study?
We will collect your blood for the purposes of this research study.

We will NOT store, use or share your samples for any future research purposes. At the conclusion of this research study, we will destroy any remaining samples.

Will you receive any individual results from tests conducted during this study?

While you are participating in the study, some tests may be performed as part of your routine medical care. The results of these tests will be entered into your medical record. You and your doctor have a right to review these results.

Will genetic testing be done using your tissue or blood samples?
We will not perform any genetic testing (or whole genome sequencing) on your tissue samples.

Will you be told about new information that might affect your decision to take part in this research?

During the study, we will tell you if we learn any new information that could affect your willingness to stay in the study.

If we learn new information about the study treatment after you have finished the study and that information could still affect you, the study doctor will get in touch with you.

What will happen if you become sick or hurt while you are in this study?
If you become sick or hurt during this study, please contact the Principal Investigator listed on the first page of this form. They will take care of you or help you get the care you need. If you require immediate medical attention, you should go to the nearest emergency room of call 9-1-1. It is important that you inform the medical staff that you are participating in this study. Take this informed consent form with you, if you can.

If a research-related injury results from your participation in this research study, medical treatment will be provided. The costs for all of your medical treatment will be billed to you and/or your insurance. A "research-related injury" means injury caused by the product or procedures required by the study which you would not have experienced if you had not participated in the research study. **You do not give up any of your legal rights by signing this form.**

If you believe you have been injured or become ill because you took part in this study, you should call the Chief Medical Officer or their representative at (856)-342-3071.

What will happen if you decide not to stay in this study?

Participation is voluntary. You can decide after signing this informed consent document that you no longer want to take part in this study for any reason, at any time. You will not be penalized or lose any benefits that you are entitled. If you decide you want to stop taking part in the study, tell the study staff as soon as possible.

- We will tell you how to stop safety.
- There are no medical consequences if you decide to stop taking part of this study.
- If you decide to stop, you can continue getting care from your regular doctor.
- We will schedule a visit with your doctor, during which you will review your medical history, the doctor will evaluate you, and you will answer a few questionnaires about your headaches. This will be your final visit related to the research study.

At any time, the study doctor can remove you from this study because it would not be in your best interest to stay in it. We may withdraw you from the study if you are not completing study tasks or coming for the study visits when scheduled. We will let you know the reason for withdrawing you from this study.

We are required by the Food and Drug Administration (FDA) to continue to report anything that is related to the safety of the lidocaine and methylprednisolone drugs used in the research. Even if you leave the study, we may need to collect additional data about you, such as medical treatments or lab results obtained through medical chart review. Public records may also be consulted, such as those establishing survival status.

Who should you contact if you have questions?

If you have any questions about the research, you may contact the Principal Investigator listed on the first page of this consent form. They are responsible for the conduct of the research at Cooper.

If you have any questions about the research or your rights as a research participant, or any complaints about the research, you may contact the Cooper Institutional Review Board (IRB). The IRB is responsible for protection of subjects participating in this research project. The address of the IRB is One Cooper Plaza, 4th Floor, Dorrance D431A Camden, NJ 08103. The phone number is (856) 757-7832.

FINANCIAL DISCLOSURE

This study is being funded by a grant from the Society of Vascular and Interventional Neurology.

CONFIDENTIALITY PROTECTIONS AND HIPAA AUTHORIZATION

We call your health information that identifies you your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). If you sign this form, you are giving the investigators, their staff, and certain other people described in this form your permission to use your protected health information for this research study.

What information about you will be collected or used?

To do this research, we will collect information about you and your health conditions. Some information about you will also be collected from your medical records. The information collected will be used to determine if you qualify to participate in this research, to follow your treatment and contact you, and to answer the research questions.

The following PHI will be collected or used as part of this research study:

- Identifiers such as your name, medical record number, and telephone numbers
- Dates, including birth date, age, admission date, discharge date, date of significant medical events, date of death
- Personal medical history including present and past medications
- Results of exams, procedures, and tests you have before and during the study
- Laboratory test results

Who will use or have access to your protected health information?

By signing this form, you are allowing the following people or groups to have access to your PHI:

- The research team, which includes the investigator listed on this form and other personnel involved in this study, in order to support the study and analyze the data.
- Others employed or contracted by Cooper, if needed for your clinical care or study oversight. To improve coordination of your research and clinical care, some information about the study may be added to your electronic medical record.
- Cooper's Human Research Protections Program, including the IRB, may look at your study records to ensure the research is being conducted appropriately.

All of these people and entities are obligated to protect your PHI.

You are also allowing your PHI to be used by or shared with other people or groups specified below:

- The Food and Drug Administration (FDA). The FDA may need to be sure the records are accurate and that the research is done according to FDA regulations.

Although these entities listed above have their own confidentiality procedures to protect your PHI, they are not covered by the same federal privacy rule, HIPAA, that governs healthcare providers, and therefore they are not bound to its regulations.

How will your information be kept confidential?
To help maintain the confidentiality of your study records, we will replace your name and any identifying information with a code. Your identifying information will be stored securely and separately from the rest of the research records. All study documents will be stored in a locked file cabinet or in a password-protected secured electronic environment. Only authorized study personnel will have access to your identifiable information.

We may publish the information from this study in scientific journals or present it at scientific meetings, but you will not be personally identified in these publications and presentations. It is possible that the data collected for this study may be useful for future research conducted at Cooper or by other investigators outside of Cooper. We will remove all of the information that identifies you, such as your name. This de-identified data may be used or shared with other investigators for future research studies without additional informed consent from you.

Please note: Healthcare providers are required to share with the New Jersey Department of Health any confirmed diagnosis of over 70 communicable diseases, including but not limited to HIV/AIDS, Hepatitis, Measles and others (N.J. Admin. Code § 8:57-1.5). If in the course of this study, you are diagnosed with any of the diseases listed under New Jersey law, your name, address, and phone number will be shared with the Department of Health. In addition, under New Jersey Law (N.J. Admin. Code § 8:40-3.7) there is a requirement for certain individuals to report any reasonable belief of child or elder abuse to the New Jersey Department of Health (DOH), and in the case of child abuse, the Division of Child Protection and Permanency (DCPP). If in the course of this study, there exists a reasonable belief of child or elder abuse then relevant contact information will be shared with New Jersey DOH and DCPP as required by law.

Do you have to give authorization for use of your PHI?
No, but if you do not give this authorization then you cannot join the study. This will not affect the medical care that you receive outside of the study.

How long will your information be collected, used or shared?
Your authorization for the collection, use, and sharing of your PHI for this specific study does not expire.

Please note that Cooper may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The Institutional Review Board grants permission
- As permitted by law

What if you change your mind?
You may revoke this authorization to use and share your PHI at any time by contacting the principal investigator, in writing, at the address listed on the first page of this form.
If you decide not to authorize the investigator to use and disclose your PHI or you revoke this authorization, you will no longer be able to participate in this research study, and the use or sharing of future PHI will be stopped. However, the PHI that has already been collected may still be used.

VOLUNTARY PARTICIPATION

- I voluntarily consent to take part in this study.
- The study staff have discussed this research study with me.
- I have had adequate time to read this form and to ask questions about it.
- I understand that, by signing this form, I am not giving up any of my legal rights.
- I agree to the use and disclosure of my protected health information for this study.
- I will be given a copy of this consent and authorization form for my records.

Signature Page for Adult Subjects

SUBJECT:
Printed Name of Subject: _____

Signature: _____ Date: _____ Time: _____

INVESTIGATOR: I have discussed the study described above with the subject.

Printed Name of Investigator Obtaining Consent: _____

Signature: _____ Date: _____ Time: _____