Permission to Take Part in a Human Research Study

Title of Research Study: Angiotensin II as a first-line vasopressor for distributive shock for heart transplant and left ventricular assist device implantation recipients: A Pilot Study

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Supported By: This research is funded by La Jolla Pharmaceuticals, Inc.

Financial Interest Disclosure
If your doctor is also the person responsible for this research study, please note that s/he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Key Information:
The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?
We are asking you to take part in this research study because you are scheduled for a heart transplant or placement of a left ventricular assist device. Because of this surgery and your underlying disease condition(s) you may have a higher risk of developing a condition called distributive shock.

Distributive shock is an abnormal distribution of blood flow in the smallest blood vessels that results in an inadequate supply of blood to the body's tissues and organs, which left untreated can result in multiple organ failure as well as life-threatening complications.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?
The purpose of the study is to find out if an FDA approved medication, Giapreza (angiotensin II), can be used as a 1st line treatment in patients who develop distributive shock during a heart transplant or placement of a left ventricular assist device. Giapreza (hereafter called study medication) is FDA approved to increase blood pressure in patients who develop distributive shock.

The priority in patients that develop distributive shock is to provide lifesaving treatment to increase pressure in the blood vessels in order to get blood circulating through the body as quickly as possible. This is routinely done by giving fluids, blood transfusions and medications, such as norepinephrine (increases the rate and force at which the heart contracts) and vasopressors (tightens blood vessels to raise blood pressure). High doses of these medications may cause serious side effects. Use of angiotensin II as a first line of treatment may have less side effects and improve outcomes.

How long will the research last and what will I need to do?
We expect that you will be in this research study for up to 30 days after your surgery. No additional study visits are required.

If during your heart surgery you develop distributive shock you will receive either the active drug, angiotensin II, or a placebo (saline – a salt water solution), administered by infusion (a slow injection by means of a tube into a vein). The placebo looks like the study medication but is not meant to treat any disease. A placebo is given to be compared with the study drug to learn if the study medication has any true effect. If you are randomized to the placebo group you will also receive standard of care treatment. You will have an equal, 50% chance (like flipping a coin) of receiving either study medication or placebo

If you do not develop distributive shock during your procedure you will not be randomized and your participation will be considered complete.

More detailed information about the study procedures can be found under the section **What happens if I say "Yes, I want to be in this research"?**

Is there any way being in this study could be bad for me?
The most commonly reported side effect of the study medication is a risk of thromboembolism, which is the formation of a clot (thrombus) that breaks loose and is carried by the blood stream to another blood vessel. The clot may plug a another vessel in the body such as the lungs (pulmonary embolism), brain (stroke) or leg (DVT).

More detailed information about the risks of this study can be found under **"Is there any way being in this study could be bad for me? (Detailed Risks)".**

Will being in this study help me in any way?
We cannot promise any benefits to you or others from your taking part in this research. However, the information collected during this study may be useful scientifically and thus be helpful to other patients in the future.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled. You do not need to participate in this study to get treatment for your condition. Your alternative to participating in this research study is to not participate.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Whom can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at (312) 926-4000. Dr. ~~Pham~~ Lewis is the person in charge of this study. Sh~~H~~e can be reached at 312-~~695~~926-~~3121~~5589. For problems arising evenings or weekends, you may call (312) ~~695~~926-~~4965~~ 9036 and ask for Dr. ~~Pham~~ Lewis or the person who is covering for Dr. ~~Pham~~Lewis.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be studied?
We expect up to 40 people here will be in this research study.

What happens if I say "*Yes, I want to be in this research*"?
If you agree to participate in the study, you will first need to sign this consent form after the study has been reviewed and discussed with you. You will be given a copy of the signed consent form to keep. Once consent has been provided the following will be done for purposes of this study:

- The study physician or research staff will review your medical history, including previous heart related events and procedures.
- Information about you, including your age, sex, and race/ethnicity will be recorded.
- Any medications you are regularly taking will be recorded.
- Your blood pressure, heart rate and weight will be recorded.

Time of Surgery
If during surgery you develop signs of distributive shock (low pressure and blood perfusion) you will be randomized to receive study medication or placebo. Study medication or placebo both labeled as concentrations of 5ug/ml will be administered through an IV continuously at a starting dose of 5 ng/kg/min. The study drug or placebo will be increased until there is consistent pressure to deliver blood throughout your body. In addition, before and after study drug administration a small sample of blood (5 mL) will be collected through your IV for research lab tests. If once the study drug or placebo is being administered at a rate of 40 ng/kg/min and your blood pressure measurements are not at the target goal the treating physician will add additional medications according to routine practice.

You, the study doctor, and study coordinator will not know which treatment you receive until the study is over. This is done so that the effects and safety of the study medication can be learned in a fair manner. In case of an emergency, your study doctor can find out which treatment you received.

You will not know if you were included in this research study until after you wake up from your surgery.

During your hospital stay
Research personnel will review records to collect information on medications, use of blood products, lab results and any adverse events that occurred since your surgery. In addition, information about your vital signs (blood pressure, pulse rate, respiratory rate) and weight will be collected from your medical record.

Day 30 Phone Call
Research personnel will call you to see how you are doing 30 days after your surgery. They will ask you about any hospitalizations or events you have experienced since leaving the hospital. This call will take about 5 minutes. If you are still in the hospital your records will be reviewed to collect this information.

What happens if I say "Yes", but I change my mind later?
You can leave the research at any time it will not be held against you.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

If you stop being in the research, already collected data may not be removed from the study database.

Detailed Risks: Is there any way being in this study could be bad for me?
The most common risks of the study medication, angiotension II, include:

- Thromboembolic events (obstruction of a blood vessel by a blood clot that has become dislodged from another site)
- Thrombocytopenia (low platelet count, can lead to bleeding events)
- Tachycardia (fast heart beat)
- Fungal infection
- Delirium (mental confusion)
- Acidosis (increased acidity in the blood and other body tissue)
- Hyperglycemia (high blood sugar)
- Peripheral ischemia (decreased blood flow to the limbs)

Risk Associated with Placebo
Saline (a salt water solution) is the placebo for this study. There is a risk your pressure will remain low during study drug administration if you are randomized to placebo. Other medications will be initiated per protocol to prevent excessive low pressure.

Risks of Blood Draw
The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: “What happens to the information collected for the research?”.

Will it cost me anything to participate in this research study?
Taking part in this research study will not lead to any additional costs to you.

The company providing funding to support this study, La Jolla Pharmaceuticals, will provide the study medication at no cost. You will not be charged for the tests and procedures that are done solely for purposes of the study.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay, including your heart surgery and standard post-surgical care. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay, including co-pays and deductibles.

What happens to the information collected for the research?
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution, the US Department of Health and Human Services, the study sponsor, sponsor’s agent and other collaborating institutions.

Monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may

publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Data Sharing
De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Can I be removed from the research without my OK?
The person in charge of the research study or the sponsor can remove you from the research study without your approval if it is in your best interest.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?
If you become ill or are injured as a result of the study medications or procedures you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

HIPAA Authorization
We are committed to respecting your privacy and keeping your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Results of physical examinations
- Medical history and details about your heart surgery and post-surgery care
- Lab tests, or certain health information indicating or relating to a particular condition
- Records about study medication or drugs

During this study you may be coming to a Northwestern Memorial Healthcare Corporation entity (for example, Northwestern Memorial Hospital, Prentice Women's Hospital) for research appointments or to get clinical services, such as lab tests, needed for the study. When that happens, you will be scheduled for these services through the NMHC computer system. When a clinical exam or lab is done by NMHC or one of its employees for the purpose of this research study, that information will be kept in both NMHC's clinical records and in the study records.

The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH).

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office].
The following entities may receive your health information:

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board.
- Clinical affiliates, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH), and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this clinical trial may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.
- Clinical affiliates, including but not limited to Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH), for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities.
- Other University research centers and University contractors who are also working on the study, including the Bluhm Cardiovascular Institute Clinical Trials Unit (University staff responsible for overseeing study conduct, data collection and database maintenance).
- La Jolla Pharmaceuticals, Inc. who is providing funding for the study.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will not expire.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

~~Duc Thinh Pham~~Choy Lewis, MD
Northwestern University Feinberg School of Medicine
Department of ~~Surgery~~Anesthesiology
25~~0~~1 E. Huron, ~~Galter~~ Feinberg Pavilion, Suite ~~11-140~~5-704
Chicago, IL 60611

You do not have to authorize the use or disclosure of your health information; however, if you do not, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure

of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

A copy of this signed consent document, information about this study, and the results of any test or procedure done may be included in your medical records and may be seen by your insurance company.

Signature Block for Capable Adult:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent