Cover Page for ClinicalTrials.gov

Document:
Informed Consent Form

Official Study Title:
Prevention of Acute Kidney Injury by Nitric Oxide in Prolonged Cardiopulmonary Bypass: A Double Blind Controlled Randomized Trial in Cardiac Surgical Patients with Endothelial Dysfunction

Document Date:
May 6, 2019

Partners HealthCare System
Research Consent Form

Subject Identification

General Template
Version Date: October 2014

Protocol Title: Prevention of Acute Kidney Injury by Nitric Oxide in Prolonged Cardiopulmonary Bypass: A Double Blind Controlled Randomized Trial in Cardiac Surgical Patients With Endothelial Dysfunction

Principal Investigator: Lorenzo Berra, MD

Site Principal Investigator:

Description of Subject Population: Adult, cardiac surgery patients

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

A description of this clinical trial is available on *https://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.

Why is this research study being done?

The kidneys are important organs that regulate the body's fluid volume and clean the blood. Patients who have heart (cardiac) surgery requiring the assistance of a heart-lung machine often sustain injury to their kidneys. In a previous study, we found that breathing nitric oxide gas during and for up to 24 hours after cardiac surgery lowers the risk of kidney injury. Nitric oxide is an FDA-approved gas commonly given to patients with lung disease and to premature babies.

Although nitric oxide gas is frequently used during cardiac surgery and in the intensive care unit at MGH, it is not FDA approved for these purposes. More than 500,000 Americans have breathed nitric oxide for therapeutic purposes and there are very few reported complications. In our prior study, we did not observe any complications.

We are asking you to participate in this study because you are scheduled to have cardiac surgery that will require the assistance of a heart-lung machine.

This research study will compare **nitric oxide** to a placebo, nitrogen gas. The placebo looks exactly like **nitric oxide,** but contains no **nitric oxide and is inactive.** During this study, you may get nitrogen gas instead of nitric oxide**.** Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.
We expect to enroll 250 patients at Massachusetts General Hospital (MGH) Cardiac Surgery.
The National Institutes of Health (NIH) is paying for this study to be done.

How long will I take part in this research study?

It is of utmost importance we follow up with you the level of your health up to 1 year after your hospital discharge. We will monitor your kidney function and the quality of your daily life after surgery. The follow up consists of a visit with a member of the study staff at 6 weeks after cardiac surgery (during the post-operative visit with your cardiac surgeon) and of 2 phone calls at 90 days after surgery and 1 year after surgery.

What will happen in this research study?

If you decide to participate, after you sign this informed consent we will:

- Review your medical chart and record some information about your health history, the medications you may take at home and the reason why you're having heart surgery
- Record existing clinical and laboratory data
- Measure and record your cardiopulmonary function by using a pulmonary artery catheter, a standard and required procedure for all cardiac surgeries. The pulmonary artery catheter will be placed by your anesthesiologist after anesthesia starts.
- Draw a total of 3 table spoons of blood as participant of this study over a period of 6 weeks.
- Collect 5 urine samples over a period of 6 weeks. The first 4 urine samples will be collected from the urine bag that you will have in place as part of the surgery. The first urine will be collected before surgery (and after the insertion of the urinary catheter), the

second at completion of the surgery, the third at 24 hours after surgery and the fourth at 48 hours after surgery. Lastly, a fifth urine sample will be collected at 6 weeks after surgery during the post-operative follow up visit at Massachusetts General Hospital (MGH).

- Assign you by chance (like a coin toss) to the nitric oxide group or the standard gas (**nitrogen gas)** group. You and the study doctor cannot choose your study group. You will have a **1 in 2 chance** of being assigned to **either**. We will start you on standard gases (oxygen and nitrogen) or nitric oxide plus standard gases (oxygen and nitrogen) once the anesthesiologist places a breathing tube. During heart surgery, the gases will be delivered to you by the cardiopulmonary bypass (heart-lung) machine. After surgery, the gases will be delivered by the breathing machine. The study gas will be delivered for up to 24 hours after surgery by the breathing machine or through nasal prongs. A licensed respiratory therapist (a health professional trained to evaluate and treat people who have breathing problems or other lung disorders) and a study doctor will be available while you breathe nitric oxide.
- Evaluate your kidney function, your quality of life (Activity of daily living and Promis score for global health) and how you recovered from your cardiac surgical procedure during your 6 weeks post-operative follow up visit at MGH and by phone call at 90 days and 1 year after surgery.

Your study information will be stored in a locked file cabinet. We will label all of your study information and blood samples with a code instead of your name. The key to this code connects your name to your study information and samples. We will store your blood samples until completion of the entire study using only a code. The study doctor will keep the key to the code here at MGH.

How may we use and share your samples and health information for other research?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

We would like to store and be able to use and share your coded samples and health information with researchers into and outside Partners for other research related to the cardio-vascular system. If we share your samples and/or health information with other researchers, we will label the samples and information with a code instead of your name or other directly identifying information. The key to the code connects your name or other identifiers to your sample and/or information. We will keep the key of the code in a password protected computer and into a locked archive.

What are the risks and possible discomforts from being in this research study?

The possible risks and discomforts that you might experience might be:

- Swelling, bruise and inflammation of the veins related to IV punctures (uncommon). To minimize risks and discomforts, blood will be obtained by experienced healthcare workers from arterial line, peripheral intravenous catheters or central venous catheters when present.
- side effects due to nitric oxide breathing. Nitric oxide is a gas with no color and no odor. If nitric oxide is breathed at very high concentration for prolong periods of time, it may go into your blood and reduce the amount of oxygen in your blood due to high levels of methemoglobin (uncommon), increasing your need to breathe. This does not usually happen. We will make sure that the oxygen in your blood is always at safe levels.
- Confidentiality risks. There is a risk that your confidential information will become known by others. We will do our best to keep all your study information in a secure, locked cabinet with limited access to study staff only. We will code all study samples after they are collected and keep the key to the code in a locked cabinet.

What are the possible benefits from being in this research study?

You may not benefit from participating in this study. If you are given nitric oxide during the study, it may reduce the risk of damage to your kidneys posed by the heart surgery that you require.
Other heart surgery patients may benefit from what we learn in this study.

What other treatments or procedures are available for my condition?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

You will **not** be paid to take part in this study.

What will I have to pay for if I take part in this research study?

There are no additional costs if you decide to be part of this study.
Study funds will pay for certain study-related items and services (like the nitric oxide gas and some of the study blood tests related to this research), however, your health insurer will be billed for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the licensed physicians part of the study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Lorenzo Berra, M.D is the person in charge of this research study.
You can call him at 617-724-5100, during office hours. Dr. Lorenzo Berra will be available 24/7 at 617-643-7733.
If nobody pick up the phone, please leave a short message with your name, reason of your call and call back number.

If you have questions about the scheduling of appointments or study visits, call Stefano Spina, MD at 617-459-7037 or Francesco Zadek, MD at 617-834-4809.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research

- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)

- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter	Date	Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name	Date	Time (optional)

Witness to Consent of Subjects Who Cannot Read or Write or are Physically Unable to Talk or Write

Statement of Witness

I represent that the consent form was presented orally to the subject in the subject's own language, that the subject was given the opportunity to ask questions, and that the subject has indicated his/her consent and authorization for participation by (check one box as applicable):

☐ Making his/her mark above

☐ Other means _____
(fill in above)

_____	_____	_____
Witness	Date	Time (optional)

Consent Form Version: 05/06/2019