Title: ACTIVATE-AKI: Activated Vitamin D for the Prevention and Treatment of Acute Kidney Injury

ClinicalTrials.gov Registration Number: NCT02962102

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Partners HealthCare System
Research Consent Form

Subject Identification

Certificate of Confidentiality Template
Version Date: January 2018

Protocol Title: ACTIVATE-AKI: Activated Vitamin D for the Prevention and Treatment of Acute Kidney Injury

Principal Investigator: David E. Leaf, M.D.

Site Principal Investigator:

Description of Subject Population: Patients in the intensive care units of Brigham and Women's Hospital who are at risk of acute kidney injury

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.

Some of the people who are eligible to take part in this study may not be able to give consent to take part because of their medical condition. Instead we will ask the person's authorized representative to give consent. Throughout the consent form, "you" always refers to the person who takes part in the study.

A description of this clinical trial will be available on *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.

Why is this research study being done?

We are doing this research study to find out if calcifediol or calcitriol, which are both forms of vitamin D, can help prevent or decrease kidney damage in critically ill patients in the intensive

care unit (ICU). Previous studies done in ICU patients have shown an association between low levels of vitamin D and greater risk of poor outcomes, including kidney damage, infection, and death. However, we do not know whether low levels of vitamin D actually cause these poor outcomes, or whether they are simply associated with them.

Calcifediol and calcitriol are both approved by the U.S. Food and Drug Administration (FDA) for the treatment of a condition called "secondary hyperparathyroidism" in patients with chronic kidney disease, but calcifediol and calcitriol are not approved by the FDA to help prevent or treat kidney damage in ICU patients.

This research study will compare calcifediol and calcitriol to placebo. The placebo looks exactly like calcifediol and calcitriol, but contains no calcifediol or calcitriol. During this study you may get a placebo instead of calcifediol or calcitriol. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

We are asking you to take part in this study because you are in the ICU and at risk of kidney injury. 150 subjects will take part in this study. Subjects will be enrolled at Brigham and Women's Hospital (BWH).

This is a pilot study. Pilot studies are done on a small group of subjects to learn if a larger study would be useful. The National Institutes of Health is paying for this research to be done.

How long will I take part in this research study?

It will take you 1 week to complete this research study. We will do all of the study procedures while you are in the hospital. You will not need to come in for any extra visits to take part in this study. After the 1 week of the study, we will continue to gather information about your hospital stay, including information such as how long you stayed in the hospital and how your health was while you were in the hospital. We will contact you and/or a family member by telephone 28 days after the start of the study to ask some general questions about your health. This single telephone call will take 2 minutes or less.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures. All of the study procedures will take place while you are in the hospital; you will not need to make any additional study visits.

Assignment to a Study Group:
We will assign you by chance (like a coin toss) to either the calcifediol group, the calcitriol group, or the placebo group. You and the study doctor cannot choose your study group. You

will have a 1 in 3 chance of being assigned to the placebo group. You and the study doctor will not know which study group you are in.

Taking the Study Drug:
The nurse will give you the study drug (calcifediol, calcitriol, or placebo). The study drug is in a liquid form. You will receive one dose of the study drug on a daily basis for 5 days. The study drug will be administered orally (by mouth, if you are able to swallow) or through a nasogastric or orogastric tube placed for routine clinical purposes. In other words, we will not place a nasogastric or orogastric tube for this study, but if one is already in place for routine clinical care, we will administer the study drug by this route.

Drawing Blood:
We will draw blood 6 times during this study: right before you receive the study drug, and every morning for the next 5 days. To minimize extra needle sticks, blood draws will take place with routine clinical blood draws when possible. We will draw about 80ml (approximately 5 tablespoons) of blood during the entire course of this study.

Collecting Urine:
In addition to blood samples, we will also collect a small sample of urine for 5 days.

Use of your Samples and Health Information:
We will test your blood to see whether there are any changes in your genes in response to the study drug. DNA is the material that makes up your genes. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work, and determine physical characteristics such as hair and eye color. There are many differences in DNA from one person to another. These differences may affect a person's chances of having a particular disease, how the disease progresses, and how severe the disease gets. Genes can also affect people's response to or side effects from medications. Genetic testing is not an optional component of this study. If you choose to participate in the study then you are also agreeing to allow your samples to undergo genetic testing.

We may also perform a whole genome analysis on your DNA sample. Usually researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and used by researchers to study links to many diseases or conditions. In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of whole genome studies. These banks may also analyze and store DNA samples, as well. These central banks will store your genetic information and samples and give them to other researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and whole genome

information with these banks. However, we cannot predict how genetic information will be used in the future. The samples and data will be sent with only your code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information and samples while they are stored in repositories and used for research.

We would like to store some of your samples and health information for future research related to kidney injury and related conditions. We will label your samples and health information with a code instead of your name. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password-protected computer. Your samples will be stored for a maximum of 25 years.

After you leave the hospital we will contact you and/or your healthcare surrogate by telephone 28 days after the start of the study to ask some general questions about your health. This single telephone call will take 2 minutes or less.

Do you agree to let us store your samples for future research related to kidney injury and related conditions?

☐ **YES** ☐ **NO** **Initials**_____

If later you change your mind and want your samples destroyed, contact the study doctor.

In the future we may think of new research ideas and projects for which separate consent will be required. If this happens, we would like to re-contact you to explain this new area of research. We would only re-contact you if you gave us permission to do so. Whether or not you allow re-contact will not affect your participation in this study, and you will not be obligated to participate in any future study. Please let us know your decision about being re-contacted by checking one of the following (check and initial):

_____ I would like to be contacted about future research projects

_____ I do not want to be contacted again for possible participation in additional research

Initials_____

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

Risks of Taking Calcifediol and Calcitriol
Calcifediol and calcitriol have been used in patients with kidney failure and in other conditions for over 30 years, and have generally been well tolerated. The main side effect of any vitamin D medication, including calcifediol and calcitriol, is elevated blood calcium levels. Elevated blood calcium levels, however, are generally observed in patients taking higher doses and a longer duration than we are doing here in this study**.**

Uncommon side effects (between 1 and 10 out of 1,000): increased urinary calcium levels; nausea/vomiting; constipation; decrease in appetite; bone pain; drowsiness (feeling sleepy); dry mouth/thirst; muscle aches; metallic taste; headache; sensitivity to light; skin rash

There may be other risks of calcifediol or calcitriol that are currently unknown. As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. We will monitor you for any symptoms of an allergic reaction.

Risks of Blood Draws
There is a small risk of infection, lightheadedness, and/or fainting during blood draws.

Risks to Your Privacy
Your health information will be labeled with a unique code instead of your name and stored on a secured computer at the hospital. Only the study investigators will have access to both the code and to the health information stored in the computer. Your biological samples may be shared with collaborators outside of the Partner's Healthcare system for measurements and analyses. However, collaborators outside of the Partner's Healthcare system will only have access to the de-identified samples and will not have access to any identifying information.

What are the possible benefits from being in this research study?
You may not benefit from being in this study.
If you are assigned to either the calcifediol or calcitriol group, it is possible that you will have less kidney damage during the study, which could result in better long-term kidney health. However, this is not guaranteed. Additionally, other ICU patients may benefit in the future from what we learn in this study.

What other treatments or procedures are available for my condition?
You do not have to take part in this research study. Other treatments or procedures that are available for ICU patients include supportive therapies such as fluids and nutrition. These other

treatments are part of your clinical care and will be provided whether or not you take part in this study.

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?

We will not pay you to take part in the study. It is possible that your samples and information could be used to develop a new product or medical test to be sold, though currently there are no plans for this. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

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

Study funds will pay for the calcifediol and calcitriol and all study-related procedures. Study funds will pay for certain study-related items and services. However, we may bill your health insurer 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 study doctors and 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.

David Leaf, M.D. is the person in charge of this research study. You can call him at 617-525-7612 during regular business hours (Monday to Friday, 9am to 5pm). You can also call David Leaf, M.D. on his cell phone at 914-419-0622 at any time (24 hours/day, 7 days/week) with questions about this research study. You can also call Sushrut Waikar, M.D., at 617-732-8473 during regular business hours.

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 857-282-1900.

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?

Federal law requires Partners to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable 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 information and why:

- Partners researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections) state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other researchers within or outside Partners, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain completely 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 identifiable information. Your permission to use and share your information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable 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 identifiable 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 identifiable 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, and such information may continue to be used for certain purposes, such as to comply with law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable 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 identifiable information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Guardian or Authorized Representative for Adult:

I give my consent for the person I am authorized to represent to take part in this research study and agree to allow his/her identifiable information to be used and shared as described above.

_____

Print Name (check applicable box below)

☐ Court-appointed Guardian
☐ Health Care Proxy

☐ Durable Power of Attorney
☐ Family Member/Next-of-Kin

_____ _____ _____
Signature Date Time (optional)

Relationship to Subject:_____

Assent

Statement of Person Giving Assent

- 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, and my questions have been answered.

Signature of Adult:

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

_____ _____ _____
Adult 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 Date: 12/25/2018