PRO - ACT: Prevention of De Novo HCV with Antiviral HCV Therapy Post-Liver and Post-Kidney Transplant

Informed Consent Document

NCT03619837

Piedmont Healthcare
RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Prevention of *de novo* HCV with Antiviral HCV Therapy Post-liver and Post-kidney Transplant

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404-605-5888

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This form will give you information about the research study for you to consider in order to agree (consent) to be in this study or not be in this study. The decision to join the study is entirely yours. If you decide to join the study you may change your mind at any point and withdraw your consent to participate. You will not lose any medical benefits based on your decision to join or not join the study. If you decide not join this study, your doctor will continue to treat you.

Take your time to make your decision about whether you want to do it or not. You may discuss this with your family, friends, your other health care providers, and the doctors here that are participating in this study. Dr. Raymond Rubin is the lead study doctor for this research study.

What is a research study?

A research study is an experiment whose purpose is to answer specific questions. For example, how does a treatment work? Is it safe?

To answer these questions, doctors and scientists need patients to agree to be part of research studies. People who do this are called “volunteers”. They are also called “subjects”. The doctor in charge of a research study is called a “study doctor” or an “Investigator”. The study doctors and scientists who run a research study are called “researchers”, and the other people who help them run the study are called the “research team”.

An Institutional Review Board (IRB) has to approve each study before it can be done at a healthcare facility. An IRB is a group of people who review studies to see if they meet federal laws and ethical standards. Their main mission is to protect subject safety. This study was reviewed by the Piedmont Healthcare IRB. They have approved it being done here.

Why is this study being done?

In this study, subjects that <u>do not</u> have hepatitis C virus (HCV) will be transplanted with livers or kidneys from donors who <u>do</u> have HCV. Medications that are used to treat HCV will be given to the study subjects shortly after transplant to protect them from developing the problems HCV can cause to the liver.

Transplanting organs from HCV viremic donors (donors that have active HCV in their blood) into HCV negative patients is considered experimental. Treating these newly transplanted patients with the medications already approved to treat patients with HCV is also experimental.

Only HCV negative patients listed on a liver or kidney transplant list, who have stated they are willing to receive an organ from at HCV viremic donor, will be included in this study. Your transplant doctor will discuss this procedure with you.

How many people will be in this study?

The plan is to include about 30 subjects in this study. These subjects will be enrolled from one of the five or six transplant centers in the United States that are participating in this study.

What will happen if you agree to be in this study?

Signing this consent form means that you agree to be in the study and are willing to be transplanted with a HCV viremic organ. You will already be on a transplant waiting list.

There are some rules you must follow during the time you are waiting for an organ to be available for you:

- You must tell your study doctor all of the information you know about your health and the medicines you are taking. There can be serious risks to your health if your transplant doctor does not have this information.

- You must keep at list of all of the medications you are taking. This should include vitamins, supplements, and medications that do not need a prescription. A complete list is needed for the 42 days before you have your transplant. Because organs become available on short notice, you should keep this list updated with the current information from the time you sign this consent form.

- There are some medicines you cannot take after you consent to be in this study. Your study doctor will need to know if you take these medications so that other ones can be prescribed. These medicines are:

    - amiodarone;
    - rifabutin;
    - rifampin;
    - carbamazepine;
    - dilantin;
    - phenobarbital;
    - oxcarbazepine;
    - St. John’s wort.

- You must ask your study doctor before you start any new medicines or supplements from the time you sign this consent form until you are finished with this study.

- Females that are pregnant or nursing are not able to participate in this study. It is very important that patients who are waiting for, or have received a transplant, do not become pregnant or father a child for the first year after organ transplant. This is the case whether they are in this study or not. If it is possible for you to become pregnant, or become a father, it is very important you use two methods of birth control or never have heterosexual vaginal sex. You should ask your study doctor about which birth control methods you should use. You should also ask your study doctor if you have questions about pregnancy. Men in this study should not be sperm donors.

What will happen when I am called in for a transplant?

When an organ from a HCV viremic donor becomes available, you will be asked if you still agree to accept this type of organ. If you agree, you will be given this consent form again to review. Below the section of this consent form that you signed when you initially agreed to participate in this study, you will be asked to sign again that you still agree to participate. If you have changed your mind and do not agree to participate any longer, you will still be on the transplant waiting list and will wait for an organ from a donor that does not have HCV.

If you do still agree to participate, you will have some pre-transplant blood testing done. If you are still eligible at this point, and the donor is one that meets the requirements for you, you will have surgery to have the organ transplanted into you.

What will happen after I have a transplant?

Following your transplant, possibly while you are still in the hospital, you will start on the antiviral medicine used to treatment HCV. This medicine is called Epclusa®. This will be started in the first week after your transplant. If the study doctor thinks it is safer to delay the start of Epclusa®, it may be started up to 4 weeks after your transplant. Your study doctor will decide the best time for you to begin. The first day you take Epclusa® is considered study “Day One”.

Epclusa® is only for you and should not be shared with anyone else. It is very important it is kept out of the reach of children and anyone who cannot read or understand the label on the bottle.

It is very important you continue to tell your study doctor everything you know about your health and the medicines you take, including supplements and medicine that do not require a prescription. No new medicines should be started without checking with your study doctor first.

If you take medicines to reduce the acid in your stomach, or if you take medicines called “statins” to lower the lipids in your blood, the doses may need to be changed

or the medicine stopped, while you are taking Epclusa®. Your study doctor will discuss this with you.

How long will I be in the study?

You will be asked to take Epclusa® for 12 weeks after your transplant. The 12 weeks are counted following the day you start Epclusa®. You will continue in the follow-up period for 24 more weeks. You will be in the study for a total of 36 weeks.

What are the study follow-up visits and activities?

The study visits and activities will be done either in the hospital, or in the transplant clinic, depending on your situation at the time. Please read through them carefully. If you cannot, or do not want to complete these visits and activities, you should not agree to be in this study.

Screening

- you will have a study visit;
- the study will be discussed with you by your doctor;
- the consent form is given to you to sign;
- if applicable, pregnancy prevention will be discussed;
- your current medications will be reviewed and if any changes will be necessary, you will be informed.

Pre-transplant (when you come in for a potential transplant)

- you will have a study visit;
- you will be given the consent form again to sign to confirm that you still wish to participate;
- your medications and health since your last visit will be reviewed;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done, including a pregnancy test;
- if applicable, pregnancy prevention will be discussed.

Post-transplant

- your blood will be tested 3 days after transplant to confirm that HCV is in your blood. If it is not, an HCV blood test will be repeated 7 days after transplant and then weekly until it is confirmed that HCV is in your blood. The Epclusa® will not begin until after it is confirmed that HCV is in your blood.

Day 1 (first day of taking Epclusa®)

- you will have a study visit (if you are in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- Epclusa® side effects will be reviewed with you;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;
- if applicable, pregnancy prevention will be discussed.

Day 3

- you will have a study visit (if you are still in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- Epclusa® side effects will be reviewed with you;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;
- if applicable, pregnancy prevention will be discussed.

Weeks 1, 2, 3, 4, 6, and 8

- you will have a study visit (if you are still in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- Epclusa® side effects will be reviewed with you;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;
- if applicable, pregnancy prevention will be discussed.
- If applicable, pregnancy test will be done at weeks 4 and 8.

Weeks 5, 7, 9, 10, 11

- you will have a lab-only visit with telephone follow-up (if you are still in the hospital it will be done at your bedside);
- your immune suppression medication doses will be reviewed and adjusted if needed;
- lab tests will be done;

- if applicable, pregnancy prevention will be discussed.

Week 12 (End of Epclusa® treatment)

- you will have a study visit (if you are still in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- Epclusa® side effects will be reviewed with you;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;
- if applicable, pregnancy test will be done;
- if applicable, pregnancy prevention will be discussed.

Week 4 after finishing Epclusa®

- you will have a study visit (if you are still in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;

Week 12 after finishing Epclusa®

- you will have a study visit (if you are still in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;

Week 24 after finishing Epclusa® (end of study)

- you will have a lab-only visit with telephone follow-up (if you are still in the hospital it will be done at your bedside);
- your immune suppression medication doses will be reviewed and adjusted if needed;
- lab tests will be done.

What if I leave the study before I am finished with all of the visits and activities?

If you stop the study early for any reason, you will need to come in to see the study doctor. This is called an Early Termination Visit. You will need to bring back any Epclusa® medication that you have.

Early Termination

- you will have a study visit (if you are still in the hospital it will be done at your bedside);
- your will be asked about any changes in your health or medications;
- your immune suppression medication doses will be reviewed and adjusted if needed;
- Epclusa® side effects will be reviewed with you;
- your vital signs, weight, height, and BMI will be measured;
- your study doctor will examine you;
- lab tests will be done;
- if applicable, pregnancy test will be done;
- if applicable, pregnancy prevention will be discussed.

We ask that you follow up a verbal withdrawal with a written confirmation by signing the Piedmont Healthcare Research Subject Authorization Revocation Letter that you will be given.

After all of the follow-up visits and activities are completed you are done with this study.

What are the side effects or risks that can happen while I am in in the study?

<u>Risks of getting hepatitis C (HCV) infection</u>

Since the donor of your transplanted organ had HCV, it is very likely you will be infected with it. If the HCV is not treated, it can damage your liver. HCV can also damage other organs, such as the kidneys. Your health can get worse and you could die from it.

The way to protect yourself from HCV infection is to take the study medication, Epclusa®. There is more than a 90% chance that Epclusa® will cure HCV very soon after you are transplanted. This can happen within 3 months in most people. Sometimes the first 12 weeks of treatment is not enough and longer treatment is needed.

There is a less than a 1% chance that HCV infection cannot be cured and will cause increasing damage to your liver. This could even make you die.

Side effects and risks from treatment of HCV

The side effects and risks that can come with taking Epclusa® are:

Likely

Previous studies with Epclusa® showed the most common side effects (10% or more) are tiredness, headache, and nausea. These are usually mild. In previous studies of Epclusa® less than 1 in 100 patients had to stop the medication early because of these problems.

Rare, but serious

Epclusa® has not yet been approved by the Food and Drug Administration (FDA) in patients who take it right after a transplant. The study doctor will watch you closely for any signs of problems. It is very important you tell your study doctor if you have any side effects or feel like you are not well while you are on this study. It is possible you might not get well and could even get worse.

Allergic reactions

It is possible that any medication can lead to all allergic reaction in a person taking it. Sometimes these reactions can be life threatening. Symptoms of an allergic reaction can include: rash; hives; itching; trouble breathing; closing of the throat; swelling of the lips, tongue, or face; and, rarely, death.

If you experience any of these symptoms, get emergent medical attention and stop taking Epclusa®. Let your study doctor know right away.

People who are already allergic to other things are more likely to have allergic reactions. Let your study doctor know if you have allergies or asthma.

Blood draws

Blood draws may cause temporary discomfort from the needle stick, bruising, fainting, and (very rarely) infection at the site of the blood draw.

Viral resistance

Previous studies have shown that treatments meant to cure HCV have also caused resistance mutations of the hepatitis C virus if it is not cured by them. These mutations have been seen in patients as long as 4-5 years after treatment. If you

are treated with Epclusa® and it doesn't work, the virus might have resistance mutations that would make treatments in the future less successful.

Reproductive risks

Females that are pregnant or nursing are not able to participate in this study. As stated previously, it is very important that patients who are waiting for, or have received, a transplant, do not become pregnant, or father a child, for the first year after transplant. This is true whether they are in this study or not. If it is possible for you to become pregnant, or become a father, it is very important you use two methods of birth control or never have heterosexual vaginal sex. You should ask your study doctor about which birth control methods you should use. You should also ask your study doctor if you have questions about pregnancy. Men in this study should not be sperm donors.

Unknown risks

There may be side effects and risks from taking Epclusa® that are not already known, or happen very rarely. You study doctor will let you know if more is learned about additional side effects and risks.

Extra care will be taken to watch for previously unknown problems. If you have any unusual symptoms it is very important you report them to your study doctor as soon as possible. There is a telephone number on the first page of this form where Dr. Rubin, or another study doctor covering for him, can be reached at any time.

Are there benefits to being in this study?

The results of this study may increase the understanding of those who work with transplantation and HCV. They may learn more about how to prevent chronic HCV infection. This may lead to more organs being available to those in need of them.

Your overall health may be improved, but this cannot be guaranteed. You might be able to receive an organ more quickly than if you waited for a donor that does not have HCV. You will be watched very closely by the study doctor and research team.

What happens if the Epclusa® does not cure the hepatitis C?

If the virus comes back while still on the Epclusa® or during the 24 weeks after the Epclusa® has stopped, your doctor will discuss with you participation in another study called the "Virologic Failure Substudy". This would involve treatment for 12 weeks with a different oral (by mouth) medication (Vosevi®) to try to cure the hepatitis C. Vosevi® would need to be started within 30 days of finding out that the Epclusa® did not cure the hepatitis C. Specifics about that study are included in a separate informed consent form which would be reviewed with you by the

study team before considering participation in that study. If you decide you do not want to participate in the other study, your doctor will review other options with you.

What are the costs of being in the study?

The study medication, Epclusa®, will be given to you free of charge. All of your other medical costs will be billed to your usual healthcare payer. The study does not pay for these costs. There are no additional charges to you related to being in the study. If you participate in the Virologic Failure Substudy, Vosevi® will be given to you free of charge. All of your other medical costs will be billed to your usual healthcare payer. The study does not pay for these costs. There are no additional charges to you related to being in the stud

Will I be paid for being in the study?

No. There is no payment for being in the study.

What other choices do I have if I do not want to be in this study?

You do not have to be in this study. It is completely up to you. Your other choices may include waiting for a HCV negative donor for your transplant.

What happens if I am injured because I was in this study?

If you think you have suffered a research-related injury, you must let Raymond Rubin, MD, or a Facility Risk Manager know right away. Their numbers are:

- Raymond Rubin, MD – 404-605-5888
- Facilities Risk Manager Piedmont Atlanta – 404-605-3832.

If you are injured as a result of being in this study, immediate necessary care, emergency treatment, and professional services will be available to you just as they are to the community generally. The cost of the treatment may be billed to you, or your insurer, just like any other medical costs, or covered by Piedmont Healthcare, depending on a number of factors. Piedmont Healthcare does not normally provide any other form of payment for injuries.

In case of injury resulting from this study, you will not lose any of your legal rights to seek payment by signing this form.

For additional information about this, you may call the Office of Research Services at 404-605-3638.

What are my rights if I am in this study?

You do not have to be in this study. It is your choice. If you decide to be in the study you can leave at any time. No matter what you choose, there is no penalty to you. It will not affect your ability to receive medical care from our institution.

If you have any questions regarding your rights as a participant in a research study, or if you are concerned or have complaints about the study, you may contact the Chairman of the Piedmont Healthcare Institutional Review Board at 404-605-3638.

What happens to the information collected about me in this study?

You will be given a separate form to sign describing how your personal health information (PHI) may be used in this study, and who may be able to review it. This is called a Health Information Portability and Accountability Act (HIPPA) form.

Your study data will be identified by a study number, or code, and your name will not be included in that data. Other personal identifiers will also be removed. The study data may be used in study reports and presented in scientific journals or meetings. It may be used for further research concerning similar treatments and diseases.

Being in a research study involves some loss of privacy. We do our best to make sure information about you is kept confidential, but we cannot guarantee complete privacy. Documentation that you are in this study will be included in your Piedmont Healthcare medical record. Others who review that medical record for your healthcare will be able to see this.

Additionally, research records can be reviewed by government agencies that have the mission of protecting patient safety. These can include the Food and Drug Administration (FDA) and the National Cancer Institute (NCI).

Your personal information may be given out if required by law.

A description of this study will be available on the internet at http://clinicaltrials.gov. This is required by federal law. This website will not have personal information about you. In the future it may contain a summary of the results of the study. You can look at this website at any time.

What samples of my blood will be stored and what tests will be done on these samples?

Some of your blood taken at follow-up visits will be stored. These are indicated on the tables of study visits and activities on previous pages of this form.

If Epclusa® does not cure the HCV, there will be a blood test done to see if the virus has mutated. Some mutations can prevent some treatments from reducing

the amount of HCV in your system. The results of these tests are for research only and the understanding of these results may have no benefit to you.

No human genetics testing will be done without your separate written consent.

If you drop out of the study before you complete it, your blood samples that we collected previously will still be stored as part of the study. At the end of the study, all samples will be held by the study for up to 2 years. They will only be labeled with your study code number and your name will not be on them.

Your samples may be used in the development of tests, products, or discoveries that may have potential commercial value. You will not be paid for this if it happens.

CONTACTS

You may contact Dr. Rubin, the Principal Investigator (study doctor) of the study at 404-605-5888:

- with questions about this research study or your part in it,
- with questions, concerns or complaints about the research study, or
- if you feel you have had a research-related injury or bad effect to the study drug

If you have any questions regarding your rights as a participant in a research study, or if you are concerned or have complaints about the study, you may contact the Chairman of the Piedmont Healthcare Institutional Review Board at 404-605-3638.

CONSENT

There are two consents needed to participate in this study. Both will be signed on this form. You will be given a signed copy of this form to keep each time you sign a consent portion. You will also be given a signed copy of the separate HIPAA authorization form for this study.

The decision to join the study is entirely yours. If you decide to join the study you may change your mind at any point and withdraw your consent to participate.

If you wish to be part of this study, you should sign, date, and time it below. When you are called in for a possible transplant, you will be asked to sign the second consent section, confirming you still wish to receive an HCV viremic organ.

I wish to participate in this research study.

_____
Subject Printed Name

_____ _____

Subject Signature Date/Time

Person Obtaining Consent Printed Name

Person Obtaining Consent Signature Date/Time

Study Investigator Printed Name

Study Investigator Signature Date/Time

STOP – PLEASE READ BELOW BEFORE PROCEEDING.

DO NOT SIGN THE FOLLOWING PART UNTIL YOU HAVE BEEN CALLED WITH AN OFFER OF AN ORGAN FOR TRANSPLANTATION.

CONFIRMATION OF ONGOING CONSENT

I have read this consent form again and confirm that I do wish to participate in this research study. I am aware I will be transplanted with an organ from a HCV viremic donor and am at risk of being infected with the HCV virus as a result.

I understand that I will be given the study medication Epclusa® with the intention of treating any HCV infection that was transmitted to me. It is hoped that this treatment will prevent me from developing chronic HCV infection. It is not guaranteed that it will be effective.

I wish to continue to participate in this research study.

Subject Printed Name

_____ _____
Subject Signature Date/Time

_____
Person Obtaining Consent Printed Name

_____ _____
Person Obtaining Consent Signature Date/Time

_____
Study Investigator Printed Name

_____ _____
Study Investigator Signature Date/Time