UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	A Trial of transplanting Hepatitis C- viremic kidneys into Hepatitis C-negative kidney recipients (THINKER-NEXT)
Sponsor:	National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)
Funder:	NIDDK
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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.

Summary

Participation

You are being invited to participate in the THINKER-NEXT research study. Your participation is voluntary. You should only participate if you completely understand what the study requires and the risks involved. You should ask the study team any questions you have about participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, contact the Institutional Review Board (IRB) at (215) 898-2614.

Purpose

This research study is being done to determine whether it is safe to give a kidney transplant from a donor with hepatitis C to a patient without hepatitis C. Hepatitis C is a virus that infects your liver, and over many years (10-30), can lead to scarring of your liver, which can develop into end-stage scarring (called cirrhosis), which could then lead to liver failure, cancer, or death. Rarely, hepatitis C can cause inflammation in other parts of your body, including your skin or kidneys. The recipient will then be given a drug called Epclusa for 12 weeks to treat hepatitis C. You are being asked to participate because you are on the kidney transplant waitlist and do not have hepatitis C. Being in the study means that you are willing to accept a kidney from a patient with hepatitis C. You will have the choice to accept or decline any organ that is offered to you while on the waitlist. Declining an offer will not affect your place on the waitlist, and only means you are not accepting a specific kidney.

Procedures

If you agree to join the study, you will be asked to complete some additional research procedures. Many of the tests that we are interested in are already being done as part of your standard healthcare. However, the additional procedures that we will do that would not normally be part of your healthcare include: a liver scan, additional blood and urine tests, monitor how you take study medication against Hepatitis C, and ask health-related questions whenever we contact you. Study funds will cover the cost of Epclusa (study medication against Hepatitis C), Fibroscan (liver scan), research visits, and research blood/urine tests.

Time

You will be actively followed in the study while you wait for a kidney transplant (~6 months but could be longer) and for 1 year after transplant. You will be contacted every three months while on the waitlist. There are a total of 11 study visits, including one screening visit to determine if you are eligible, and 10 visits in the peri- and post-transplant setting. Outside of the screening visit, these visits will be scheduled to coincide with your regular post-transplant visits

Risks & Benefits

The risks of participation related to receiving a hepatitis C positive kidney are liver problems, side effects of Epclusa, allergic reaction, resistance to treatment and reproductive risks. A potential benefit is that you may receive a kidney transplant sooner than you would have if you chose to wait for a kidney without hepatitis C.

Alternatives to Participation & Other Information

We encourage you to discuss this study with your physician. If you decide not to enroll in this study and wait for a kidney transplant from a donor who does not have hepatitis C, your healthcare and your position on the waitlist will not be impacted. Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, and other possible risks not discussed here. You are free to decline or stop participation at any time during or after the initial consenting process.

If you are interested and would like more details, please read below. A study team member will discuss this form with you which contains more specific information about the THINKER-NEXT study.

Why am I being asked to volunteer?

There is a major shortage of available kidneys for kidney transplantation. The waiting time for a kidney transplant can be very long. In the Mid-Atlantic region, patients typically wait 3–7 years (and sometimes longer) for a kidney transplant from a deceased donor.

We are asking you to consider joining a study where kidneys from donors infected with hepatitis C will be offered to people like you who do not have hepatitis C. Hepatitis C is a virus that infects your liver, and over many years (10-30), can lead to scarring of your liver, which can develop into end-stage scarring (called cirrhosis), which could lead to liver failure, cancer, or death. Rarely, hepatitis C can cause inflammation in other parts of your body, including your skin or kidneys. By participating in this study, you will potentially be offered a kidney from a donor with hepatitis C, which may allow you to receive a kidney transplant sooner than you would otherwise. It is also possible that participation in this trial might enable you to receive a transplant from a younger donor (kidneys from younger donors are usually considered ‘better’), because kidney donors with hepatitis C virus are usually under 50 years of age. It is important to note that in some cases, receiving dialysis treatment over many years may be just as risky as the complications of infection with hepatitis C as the annual risk of dying on dialysis among waitlisted patients may exceed 5% each year.

If you choose to take part in this research study, it is possible that you may have the opportunity to accept a hepatitis C kidney (i.e., the donor has active infection with hepatitis C) from a deceased donor before a non-hepatitis C kidney becomes available. If you decide to take part in this study, and a hepatitis C kidney becomes available, you will still have the option to accept or decline the organ at the time it is offered to you. Likewise, if you are offered a kidney from a non-hepatitis C donor first, you are still allowed to accept it.

We estimate at least 400 subjects (i.e., formal term for a patient that participates in a research study) will consent to participate in this study with 200 being enrolled across 9 sites. We anticipate that 40-50 subjects will take part within the University of Pennsylvania Hospital System (UPHS)/University of Pennsylvania (UPenn) School of Medicine and at each of the other 8 individual sites.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will ask you to read this consent form carefully. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

Each year more than 35,000 patients with end stage kidney disease (ESKD) are added to the transplant waiting list, but there are only about 14,000 kidney transplants from deceased donors performed each year. Because there are not enough kidneys available for all the people who need them, average waiting times for kidney transplantation are over five years, if not longer, especially for patients with blood types A, B, or O.

One potential option to increase the number of available kidneys is to allow patients without hepatitis C to accept a kidney from a donor infected with hepatitis C.

The purpose of this study is to determine whether it is safe to give a kidney transplant from a donor with hepatitis C to patients without hepatitis C, as measured by: 1) the rate of curing hepatitis C in patients receiving one of these kidney transplants; 2) kidney function of recipients of a kidney from a donor with hepatitis C; and 3) other potential complications (such as other viral infections).

In this study, recipients who receive a kidney infected with hepatitis C will be treated after transplant with pills that combine two medications: Sofosbuvir/Velpatasvir (Epclusa™). This treatment has been approved by the FDA in the US for the treatment of chronic hepatitis C in adults.

The National Institute of Diabetes, and Digestive and Kidney Disease (NIDDK) is the Sponsor of this study, and the study drug Epclusa is being paid for by Gilead, the company that makes Epclusa.

How long will I be in the study?

Participants will be in the study while they wait for a kidney transplant (estimated to be up to 12 months, but could be longer) and for approximately 1 year after they get a kidney transplant to allow us to follow-up the subjects' health before and after transplant.

After transplantation, we will ask you to make up to 10 study visits to Penn Transplant Institute at University of Pennsylvania Health System. Some of the study visits will occur while you are in the hospital after your kidney transplant, and most of the visits will overlap with your post-kidney transplant visit schedule. Additional visits may depend on your treatment course determined by your study doctors.

We also intend to collect long-term outcome data beyond the visits above through review of your medical records for up to five years. We will passively monitor your care through your medical record in order to identify and track problems with your organ function or other health problems that may develop, related to your transplant and study participation.

What am I being asked to do?

This study will offer enrollment to eligible patients at the University of Pennsylvania Health System. Of those enrolled, we anticipate that some will receive a kidney transplant from a donor with active hepatitis C infection (this means a donor with current infection with hepatitis C that can be detected, which is different than a donor with a previous hepatitis C infection). We believe that all the patients who get a transplant from a donor infected with hepatitis C will develop hepatitis C and thus require treatment.

Within 1-3 days after receiving a kidney transplant from a hepatitis C-infected donor (but likely in the first few days), subjects will be treated with Epclusa (treatment duration is 12 weeks). In this consent form, we sometimes refer to kidneys from donors with active hepatitis C infection as “Hepatitis C RNA-positive.”

While you are on the waiting list, we will also monitor your health by reviewing your medical record monthly and contacting you every three months to ask you questions about your health.

This study involves three (3) phases:

Phase 1: Screening

The screening period is the period of time when it is determined if you are eligible to be in the study. This will take place before your wait listing status is changed to be eligible to receive a kidney from a donor infected with hepatitis C. During screening, you will review and sign this consent prior to any study procedures. Some of the exams, tests, or procedures may have already been done as part of your routine care. If you have had some of these tests done already, they may not need to be repeated. This decision will be up to your study doctor. The screening procedures may take up to 3 hours and includes the following:

- A complete physical exam
- Review medications
- Assessment of current health status
- Blood sample collection
    - to measure blood counts and to test the function of your organs such as your kidneys and liver
    - for a pregnancy test (for women who are able to have children). This is in case you are unable to provide a urine sample for a urine pregnancy test.
    - for research purposes (this may include tests to assess your immune responses to hepatitis C virus)
    - Testing for hepatitis B, hepatitis C, and HIV if they have not been performed within the pre-specified time period.
- Transient elastography (FibroScan®), which is a rapid, non-invasive, method to evaluate liver fibrosis (scarring) by measuring liver stiffness. A pulse is generated at the skin surface using a probe placed on your side, which is spread through the liver. If your laboratory results show you are unlikely to have liver scarring, you may not need a FibroScan.

Phase 2: Waiting List

Following screening, if you are determined to be eligible for the study, we will change your transplant records to show that you are willing and eligible to receive offers for kidneys from donors infected with hepatitis C (hepatitis C RNA positive). You will remain on the kidney transplant waiting list. During that time, you will still be able to receive offers of kidneys from donors without hepatitis C.

During this period, we will review your medical records monthly and call you every three months to ask you about your health, whether or not you have been hospitalized or if you had any new health problems discovered.

If you do get an offer of a kidney, you can decide with your doctor whether you want to accept the kidney based on characteristics of the kidney, donor-recipient compatibility, and other factors discussed at the time of any kidney offer.

If you do not get a kidney transplant from a donor with hepatitis C during the study period, or if you get a kidney transplant without hepatitis C, then you will not need any treatments or treatment-related study visits. We will review and collect information from your medical records to monitor your health for up to five years.

If you do get a kidney transplant with hepatitis C, then you will need to come to study visits that take place the same day as your regular visit with your doctor. We will closely monitor your health and treat you for the infection. Then you will enter Phase 3 of the study, which we describe next.

Phase 3: Transplantation

We will monitor your blood for hepatitis C infection. We expect that almost everyone in the study who receives a hepatitis C infected kidney transplant will become chronically infected with the virus. We will begin treatment for hepatitis C soon after transplant with a hepatitis C infected kidney. You will receive treatment (Epclusa) at no cost, outside of the study protocol.

At the time that the donor's kidney is removed or around the time it is placed in you, the kidney transplant surgeons will take a very small biopsy of the donor kidney. The pathology specimen (microscopic piece of your kidney) will be shipped with your unique study ID to pathologists at a centralized pathology lab with pathologists trained to analyze tissue samples per study protocol. The pathologists there will transfer the microscopic image on the slide to a digital image using your unique study ID. This digital image will be used for analyses for the study, and for future research studies, with your permission. In addition to having the pathology of your kidney reviewed, it is also possible that we will perform other sophisticated testing of your kidney such as single cell RNA sequencing. The original pathology specimen (a microscopic piece of the donor kidney) will then be returned to your transplant center. A similar process will be followed for any additional biopsies that are performed "for cause" (e.g., if a patient has possible rejection and needs a biopsy) or due to your center's usual program of post-transplant care, but no other kidney biopsies will be specified as part of the study procedures.

Study Drug

After transplantation, study participants with hepatitis C will receive treatment with Epclusa 1-3 days after transplantation with a hepatitis C infected organ. This study drug includes the combination of two medications against hepatitis C, virus-Sofosbuvir and Velpatasvir (Epclusa). One pill taken once daily at the same for 12 weeks. We will supply enough study drugs at each visit to last until your next visit.

If by chance your hepatitis C is not cured after receiving Epclusa for 12 weeks, then you will be provided with a second hepatitis C virus treatment regimen. (Sofosbuvir/Velpatasvir/Voxilaprevir [Vosevi] which will be provided free of charge by Gilead).

Epclusa works by blocking the hepatitis C virus from multiplying in your body. In studies of patients with hepatitis C who had not received a kidney transplant, cure rates using these medications have been over 98%.

The drug will be provided by Gilead, the manufacturer of the medication.

The cure rate of Epclusa has not been established in large studies of hepatitis C negative patients who undergo kidney transplantation and become infected with hepatitis C from the kidney. However, pilot studies suggest that cure rates should be 95-100%. Additionally, studies have shown that patients with known hepatitis C and chronic kidney disease (including being on dialysis) who receive Epclusa have similar cure rates of patients without kidney disease. The safety and tolerability of Epclusa after kidney transplantation has been studied and have shown limited adverse events.

Epclusa has been approved by the Food and Drug Administration to treat all six major types of hepatitis C virus. It was chosen for this study because it can be safely used for the treatment of all types of hepatitis C virus infection in patients with severely reduced kidney function. As a result, if your kidney function has not fully recovered when treatment is initiated after transplant, Epclusa can be safely given to you.

Other Medications

You will continue to take all the other medications prescribed by your doctor during the study. Your medication list will be reviewed during the screening visit and approved if you are eligible for the study. It is extremely important to provide an accurate list of all your medications (prescribed, over-the-counter, and herbal) at each visit and to take them as directed. However, we will not supply other medications as part of the study.

VISIT SCHEDULE FOR RECIPIENTS OF A KIDNEY FROM A HEPATITIS C VIRUS-INFECTED DONOR

Study Visit 1: Peri-transplant visit (prior to transplant when the kidney is offered)

Your physician will assess your health and make a judgment on whether transplantation is safe based on several factors. The treating transplant physicians will contact study staff about the suitability of the candidate, donor, and donor kidney for the THINKER-NEXT study. The following research activities will take place:

- Record your current medications
- Discuss any pain or medical issues
- Take a blood sample
- Take your vital signs and have a physical examination
- If female of childbearing age, a urine or blood pregnancy test will be done
- Decide if the donated kidney is suitable for you

Visits 2-10: Post transplant

Visit 2: Post-kidney transplant and Day 1 of Epclusa treatment (post-transplant day 1-3)
The following research activities will take place: discuss any pain or medical issues, record current medications, take a blood sample, take vital signs, a physical examination, a urine or blood pregnancy test (if necessary), start Epclusa treatment with a 2-month supply of pills, and schedule your follow-up visits.

Visit 3: In-person visit (1 week after start of Epclusa)
Visit 3 should occur one week (±3 days) after starting Epclusa and should immediately follow your regularly scheduled post-transplant follow-up visit. The following research activities will take place: discuss any pain or medical issues, record current medications, take a blood sample, take vital signs, a physical examination, a urine or blood pregnancy test (if necessary), count your Epclusa pills, confirm follow-up visits, and refill the study drug, if necessary.

Visit 4: In-person visit (4 weeks after start of Epclusa treatment)
Visit 4 should occur 4 weeks (±3 days) after you start taking Epclusa. If possible, this visit should follow your regularly scheduled post-transplant follow-up visit. The following research activities will take place: discuss any pain or medical issues, record current medications, take a blood sample, take vital signs, a physical examination, take a urine sample, a urine or blood pregnancy test (if necessary), count your Epclusa pills, give out 4 more weeks of Epclusa and confirm follow-up visits.

Visit 5: In-person or telephone visit (8 weeks after start of Epclusa treatment)
Visit 5 should occur 8 weeks (±3 days) after you start taking Epclusa. This visit can be via telephone/tele-health or in person where we will discuss any pain or medical issues and record current medications. You will also be required to go to the lab to take a blood sample.

Visit 6: End of Epclusa treatment visit (12 weeks after start of Epclusa treatment)
Visit 6 should occur about 12 weeks (±7 days) after starting Epclusa. If possible, this visit should follow your regularly scheduled post-transplant follow-up visit. The following research activities will take place: discuss any pain or medical issues, record current medications, take a blood sample, take vital signs, a physical examination, take a urine sample, a urine or blood pregnancy test (if necessary), count your Epclusa pills, and confirm follow-up visits.

Post-Treatment Period

The purpose of the following visits is to monitor and treat you for side effects from the infection and cure. These study visits will take about an hour and will follow your regularly scheduled post-transplant visit whenever possible.

The Post-Treatment Period will begin the day following the last dose of Epclusa.

Visit 7: Telephone encounter or in-person visit (4 weeks after end of Epclusa treatment)
Visit 7 should occur 4 weeks after you stop taking Epclusa (±7 days). Note that this visit can be an in-person visit to the study site, if necessary/possible. The following research activities will take place: discuss any pain or medical issues, record current medications, and confirm follow-up visits. You will also be required to go to the lab to take a blood sample.

Visit 8: In-person visit (12 weeks after end of Epclusa treatment)
Visit 8 should occur 12 weeks after you stop taking Epclusa (±14 days). If possible, it should immediately follow your regularly scheduled post-transplant follow-up visit at the study site and allow study staff to measure your sustained virological response at 12-weeks – the typical definition for being cured is that hepatitis C virus is undetectable at 12 weeks after the last dose. The following research activities will take place: discuss any pain or medical issues, record current medications, take a blood sample, take a urine sample, and confirm follow-up visits.

Visit 9: In-person visit (24 weeks after end of Epclusa treatment)
Visit 9 should occur 24 weeks (±28 days) after you stop taking Epclusa. If possible, the visit should follow your regularly scheduled post-transplant follow-up visit and allow study staff to measure your blood for the infection. The following research activities will take place: discuss any pain or medical issues, record current medications, take a blood sample, take vital signs, a physical examination, take a urine sample, and confirm follow-up visits.

Visit 10: In-person visit (1 year post-transplant, "end of study" visit)
Visit 10 should occur 1 year (±28 days) after your kidney transplant and is the last study visit. If possible, the visit should immediately follow your regularly scheduled post-transplant follow-up visit and give study staff the opportunity to perform an end of study evaluation. The following research activities will take place: discuss any pain or medical issues, record current medications, and take a blood sample, take vital signs, a physical examination, take a urine sample.

Research blood samples: Throughout the study, we will collect blood samples (about 1-5 tablespoons at each collection) to measure for presence of the hepatitis C virus, along with kidney and liver function. This will be coordinated with blood tests for the transplant team. This will usually not require an additional needle stick but will involve additional tube(s) of blood. In rare situations if it is not possible for you to go to your usual clinic for blood samples, you may be given the option to go to an external national lab service for blood work.

Research urine samples: Periodically throughout the study, we will collect urine samples to measure for presence of excess protein in the urine. This will be coordinated to coincide with timing of blood tests for the transplant team.

Additional visits: These will only be necessary if the treatment does not cure you of hepatitis C. In that case, we will provide you with an additional course of hepatitis C virus treatment free of charge to you. If required, this additional course of treatment will follow the same schedule as the Epclusa treatment.

Future research:
De-identified blood samples, samples of the cells in the blood, kidney tissue samples, and/or urine samples collected for research purposes from subjects may be sent only to qualified investigators for their research. These samples may include information such as sex, age, health history, or ethnicity. As discussed above, slides (or digital images of slides) of your donor kidney will be sent to centralized pathology lab as part of this study for analysis. There is the potential for these slides, or sample (for example, single-cell RNA sequencing) to be used for future research studies. Such slides will be stored without direct patient identifiers and will be labeled using your unique study ID. If future contact with you is needed after this study has ended, you must consent to allow contact after the study has ended.

Some future studies may need additional health information (such as smoking history or present health status) that may require contacting you to obtain further information.

NIDDK Central Repository:

At intervals during the study or at the end of the study, once analyses have been completed, samples and study data will be transferred to the NIDDK Central Repository, a research resource supported by the National Institutes of Health. The Repository collects, stores and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research for this study and health related research in the future, after the current study is completed. Sending samples to the repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases.

What are the possible risks or discomforts?

The main risk of this study is that you will become infected with hepatitis C. The main potential benefit of this study is that you could get a kidney transplant sooner than if you only accept offers of kidneys from donors without hepatitis C infection.

1. <u>Risks related to transplantation with a hepatitis C kidney</u>

Liver problems

You should know that it is possible that the treatment for hepatitis C may not work as well in the setting of an acute hepatitis C infection. It is also possible that after kidney transplant, a hepatitis C infection could cause you serious health problems, including liver failure or death. Hepatitis C can rarely cause severe liver inflammation in the first few weeks to months after infection, or the virus can cause scarring and failure of your liver over many years.

In the short term, infection with hepatitis C can cause a flu-like illness that includes fatigue, nausea, fever, abdominal pain, vomiting, joint pain, and jaundice (yellow skin). In very rare circumstances, acute infection with hepatitis C can cause severe inflammation or even liver failure, including a condition called fibrosing cholestatic hepatitis. The risk of this complication in patients without hepatitis C who receive a transplant from a donor with hepatitis C is unknown, but pilot trials suggest that the risk is low. This complication can be treated and cured in some cases with the study medication the investigators will be providing.

Liver failure can cause someone to experience leg swelling, yellow skin, uncomfortable feelings of itchiness, bleeding, breathing problems and the abdomen to fill with fluid. Liver failure can also cause death. Based on the limited data available, we believe that it would be rare for someone in the study to experience liver failure in the first months after transplantation, when we would give treatment.

If your hepatitis C cannot be cured with the first-line and second-line treatments through this trial, over many years, there may be continued inflammation and scarring of your liver that over many years can lead to cirrhosis and eventually liver failure. Longer-term infection with hepatitis C increases the risk of developing liver cancer, liver failure requiring a liver transplant, or death.

Additional risks of hepatitis C:

Hepatitis C can cause other types of inflammation in your body, such as arthritis, rash, anemia and inflammation damage to your kidney transplant. However, these problems should respond to effective treatment for the virus. There may also be a small risk of developing Focal Segmental Glomerulosclerosis (FSGS) after receiving a kidney from a donor with hepatitis C. FSGS is a disease that harms the filters of the kidney and causes a patient to lose protein in their urine. However, this condition can also develop in patients who do not have hepatitis C.

Long term, FSGS may cause kidney failure. After transplant, we will monitor all patients for conditions like FSGS.

2. <u>Risks related to study medication</u>

Side effects from medication:

When receiving treatment for hepatitis C, you may have side effects. Everyone taking part in the study will be watched carefully for any side effects. Side effects may be mild or serious. You should talk to your study doctor about any side effects that you experience while taking part in the study. If you are injured for any reason while you are in the study, you should tell the treating doctor or hospital that you are taking part in the study.

Side Effects of Epclusa and Vosevi

Both Epclusa and Vosevi can cause serious side effects, including reactivation of Hepatitis B infection. You will not be eligible to participate in this study if you are infected with the Hepatitis B virus. The most common side effects of Epclusa and Vosevi were fatigue, headache and nausea (occurring in approximately 1 in 10 patients). Less common side effects include: diarrhea, insomnia, arthralgia (join pain), pruritus (itching), rash, shortness of breath, and anemia. Less than 1 in 100 patients had side effects so severe that they had to stop treatment due to a side effect. If a patient is taking amiodarone (medication for an abnormal heart rhythm) at the same time he/she is taking Epclusa or Vosevi, then the patient could develop a slow heart rate (bradycardia) that rarely could require a pacemaker or lead to death.

Tell your healthcare provider right away if you get any of the following symptoms or if they get worse during treatment with Epclusa or Vosevi:

- loss of appetite
- yellowing of your skin or eyes
- nausea and vomiting
- color changes in your stool
- feeling tired or weak

There may be other side effects that have not yet been described including severe allergic reaction. It is also possible that taking medications to prevent your immune system from rejecting your kidney transplant (also known as immunosuppression) at the same time as Epclusa or Vosevi might change its effectiveness or side effects.

3. <u>Risks related to study procedures and tests</u>

Undergoing FibroScans®

If required based on laboratory results, the FibroScan® technique will be used to measure the amount of liver fibrosis (scarring) in a non-invasive and painless manner. Performed at the bedside in clinic, a machine will generate a pulse wave at the skin surface, which will spread through the liver. The speed of the wave will be measured by ultrasound. In general, the whole examination process can be completed within 10 minutes. This Fibroscan will be performed by technical personnel and/or a liver doctor and the results will be reported to the investigators. There are no potential discomforts or risks involved with the FibroScan® procedure or alternative procedures such as ultrasound elastography and MR elastography.

Blood Drawing
The potential risks of the needle stick to draw blood include pain, bruising, bleeding, fainting, and infection. Discomfort from this procedure is generally short lasting, and serious side effects are extremely rare. Some people experience feelings of lightheadedness or dizziness after having blood drawn. The amount of blood drawn will be within the limits allowed for adult participants.

Kidney biopsy
The kidney biopsy will be performed as an open biopsy, meaning the transplant surgeon will have direct visualization of the kidney and the kidney biopsy site. The most common complication of a kidney biopsy is bleeding. The bleeding can take place as blood in the urine which usually stops on its own in a few days, and more rarely, a hematoma (a collect of blood around the kidney). Rarely the bleeding is severe enough to require a blood transfusion, and rarely the hematoma (collection of blood) can become infected and require antibiotics, or even more rarely, require surgical drainage. If the biopsy damages the walls of a blood vessel (artery and vein), it can cause an abnormal collection (fistula) that forms between the blood vessels that almost always heals on its own, and rarely requires an interventional procedure to repair.

Risk of Stored Samples
There may be confidentiality risks associated with the storage and analysis of your samples or the information resulting from the analysis of your samples. For example, if future research involves genetic testing there's a potential risk associated with the release of private health information, though every effort will be made to maintain your confidentiality.

Discovery of health problems during screening
During screening for this study, we will examine you and perform some blood tests. It is possible that by doing these studies we may identify new health problems that you weren't aware of. If we discover new health problems, we will answer your questions and try to arrange appropriate treatment if any is needed. If new health problems are discovered, it is possible that you would not be able to enter this study. It is also possible that you would no longer be eligible for kidney transplantation based on the results.

Reproductive risks
Because the effect, if any, of Epclusa™ on an embryo or fetus (developing baby still in the womb) is not known, you may not participate in this study if you are pregnant, breastfeeding, or planning to become pregnant. You must agree not to get pregnant during the study. If you are a woman who is able to become pregnant, you will be required to take a urine or blood pregnancy test to make sure that you are not pregnant before receiving your first dose of study drugs. If you are a woman who is able to become pregnant, you must agree to use highly effective birth control.

We define highly effective birth control the same way that the transplant program does. Notably, the use of transplant anti-rejection drugs can cause birth defects. For the purposes of this study, adequate birth control means one of the following:

1) sexual abstinence, or;
2) a vasectomized partner, or;
3) an intrauterine device (IUD), or;

4) a barrier method such as a condom, or;
5) diaphragm with spermicide PLUS a condom.

Hormonal forms of birth control including birth control pills, vaginal rings (like NuvaRung), implants (like Implanon), or injections (like Depo-Provera) may not work during treatment with Epclusa™ and you could become pregnant. After you have stopped taking Epclusa™ for at least two weeks, you can begin to use a hormonal form of birth control.

If you suspect that you have become pregnant, you must notify the study doctor immediately. *If you become pregnant during the study, it is important that you tell us right away.*

<u>All men and women</u> in the study who are sexually active must ALSO use a barrier method of contraception – such as condoms - while they are in the study and while they have hepatitis C. Although it is rare, hepatitis C can sometimes be spread through sex. Barrier contraception during any sexual activity is important to keep your partner from being infected with the virus.

What if new information becomes available about the study?

In addition to the risks described above, there may be unknown risks, or risks that were not anticipated, associated with being in this study. If new information becomes available about the study drug that might affect your willingness to continue participation your study doctor will inform you immediately and will discuss with you whether you want to continue to participate in the clinical study.

You may be asked to sign a revised consent form if this occurs. You have the right to decide either to continue with the clinical study or to withdraw.

What are the possible benefits of the study?

The main benefit of the study is that you may receive a kidney transplant earlier than you would have if you chose to wait for a kidney without hepatitis C. Receiving a kidney transplant earlier might allow you to avoid time on dialysis or time with very little kidney function, and improve your quality of life. Also, receiving a kidney may increase your overall lifespan by decreasing your risk of dying while on dialysis.

What other choices do I have if I do not participate?

We encourage you to discuss this study with your physician and to explore other treatment options. Other treatment options include not enrolling in this study and waiting for a kidney transplant from a kidney donor who does not have hepatitis C.

However, if you decide not to join the study, you may instead remain on dialysis for years and may suffer health consequences from dialysis, including death or heart problems.

Will I be paid for being in this study?

You will not receive any form of payment for your participation in this study.

Will I have to pay for anything?

Study funds will pay for certain study-related items and services including Epclusa (and second-line therapy with Vosevi if first-line therapy with Epclusa does not cure your hepatitis C), Fibroscan, research visits and research blood/urine tests.

You/your health insurer will be responsible for the cost of kidney transplant, clinical visits and procedures, and anti-rejection medications because this would be needed for your care even if you are not in the study.

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 Financial Services about these costs.

What happens if I am injured from being in the study?

We will offer you the care needed to treat any injury that directly results from the study drug or study procedures. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get from 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.

We are committed to offering you treatment for hepatitis C infection during the study. We expect that these treatments are likely to cure you of the infection. However, it is possible that treatment will not cure the infection and that you would develop health complications. Once the study ends, we would expect you to seek appropriate treatments for hepatitis C infection through your insurance or private means.

When is the Study over? Can I leave the Study before it ends?

If you receive a hepatitis C positive kidney and you choose to stop taking Epclusa treatment, there is a serious risk that you could get chronic hepatitis C infection. Because of this, if you decide you want to stop taking part in this study, we would set up a meeting with a team of your doctors and nurses and your family or close friends to discuss the risks of stopping the Epclusa treatment and try to address any problems that are causing you to want to drop out of the study.

This study is expected to end after all participants have completed all visits, and all information has been collected. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely. It is important to tell the study doctor if you are thinking about stopping so that your doctor can evaluate any risks and discuss what alternative follow-up care and testing could be most helpful for you.

Reasons for Stopping Study Medication

If you are not responding to the study medication (checked frequently by measuring the levels of hepatitis C in your blood) or develop a potential life threatening complication from the medication, we will stop the study medications completely. However, you will still be followed but less frequently. Regardless of the stage of liver disease, the recommendations are to treat hepatitis C if medically possible, however some physicians might choose to wait and not treat in the immediate future.

Reasons for Withdrawal or Study Discontinuation

Your involvement in this study is entirely up to you. You may leave the study at any time and for any reason. Withdrawal will not interfere with your future care. If you decide to leave, we may ask you to return for a final visit to perform tests and exams to ensure safety. However, you will not be required to return for this visit.

You may be discontinued from the study (taken off the study without our asking for your permission) if:

- You become pregnant while undergoing treatment with Epclusa. Therapy will be stopped as there are no safety data of Epclusa during pregnancy. Patients will continue with the regularly scheduled study visits, but will not be eligible to receive continued Epclusa therapy.
- We cannot locate you, or if you miss multiple visits or study drug doses.
- You develop a condition that it is life threatening or any other significant risk as judged by the Investigators.
- We or your primary care provider believe that it is in your best interest to stop taking the study medications even if the criteria required for stopping treatment have not been met.
- Epclusa is no longer produced by the company, or if a decision is made to stop the study.

Who can see or use my information? How will my personal information be protected?

Your medical records will be kept confidential to the extent allowed by the law. Your name or any other data that might identify you will not be used in any reports or publications resulting from this study. Because of your consent to participate, your medical records may be reviewed by the study Sponsor and by the site's Institutional Review Board (the group that is responsible for making sure that the study follows the guidelines for the protection of human research subjects) with the understanding that these records will be used only in connection with carrying out obligations relating to this clinical study. We will also give information about you to your personal doctors. You may change doctors whenever you like, but we need to have a doctor with whom we can communicate about you. We would not ask your permission for each of these contacts.

Data from this study will be entered into a computerized database through a secured website. Only authorized personnel using a password will be permitted to enter and access data. You will not be identified by name or medical record number in the study database. Each patient will be assigned a unique study ID code for identification. Records linking the study ID code with any personal identification information will be kept by the study team in a locked area.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by the 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.

What may happen to my information and samples (biospecimens) collected on this study?

Your samples may be used to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone. The National Institutes of Health (NIH) will not benefit financially from your samples.

Whole genome sequencing will not be conducted on your samples. Whole genome sequencing involves analyzing your entire personal genetic code.

Your information and samples will be de-identified. We will label your stored samples with a code that only the study team can link to you. We might send your samples to other investigators for their research, without any information that can identify you. We might also share information such as your sex, age, health history, or ethnicity. The information and samples could be stored indefinitely and shared for future research in this de-identified fashion which is explained more on the last page of this document and also requires your specific consent.

It would not be possible for future researchers to identify you as we would not share any identifiable information about you with future researchers. This can be done without again seeking your consent in the future, as permitted by law. The future use of your information and samples only applies to the information and samples collected on this study.

Future research that uses your samples will probably not help you, but it may help us learn more about how to treat or prevent hepatitis C and other health problems related to transplant. In general, the research tests we perform are not like routine medical tests, and may not relate directly to your medical care.

There may be confidentiality risks associated with the storage and analysis of your samples or the information resulting from the analysis of your samples. For example, if future research involves genetic testing there's a potential risk associated with the release of private health information, though every effort will be made to maintain your confidentiality.

What information about me may be collected, used, or shared with others?

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Personal medical history
- Current and past medications or therapies
- Information from a physical examination that generally also includes your weight, blood pressure reading, heart rate, breathing rate and temperature

- Results of tests and procedures you will undergo during this research study as described in the informed consent form.
- Medical record number
- Any other unique identifying number (such as study ID number linked with your medical records in a separate research file)
- Dates directly related to you, such as your birthdate, dates of hospitalizations, tests, and procedures
- Name, telephone number, fax number, and email addresses may be collected in order to contact you

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- Do the research
- Oversee the research
- To see if the research was done the right way.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The Principal Investigators and the Investigators' study team at the University of Pennsylvania Health System
- Investigators who are analyzing the data at the UPenn School of Medicine including members of the Data Coordinating Center at the Clinical Research Computing Unit (CRCU)
- Authorized members of the workforce of University of Pennsylvania, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

What is a Certificate of Confidentiality?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.
It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected

Who, outside of University of Pennsylvania Health System and UPenn School of Medicine might receive my information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- Your information may be sent to Gilead, its authorized representatives, the FDA, all of which will be sent anonymously. Your information will also be sent to labs performing analyses for the study.
- National Institute of Diabetes, and Digestive and Kidney Disease (NIDDK) who is the funding agency for this study will review study information, all of it an anonymous fashion.
- All research centers participating in the study, even if they are not a part of the UPenn School of Medicine, may receive information about your medical record but this information will not include any confidential identifying information about you.

Regulatory and safety oversight organizations

- The Food and Drug Administration
- The Office of Human Research Protections

Once your personal health information is disclosed to others outside the UPenn School of Medicine, it may no longer be covered by federal privacy protection regulations. The Principal Investigators or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

City of Philadelphia Health Department/PA Department of Health
If you test positive for Hepatitis C, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have hepatitis C virus infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with hepatitis C virus. The Health Department does not share the names of hepatitis C virus infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of hepatitis C virus infections to the federal government.

How long may University of Pennsylvania Health System and the UPenn School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the UPenn School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

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

Can I change my mind about participating in the study?

Yes. You may withdraw consent to continue participation in the study at any time. You do this by sending written notice to the investigators for the study. If you withdraw your permission, you will not be able to stay in this study. When study researchers receive written instructions from you to withdraw consent to continue participation in the study, they will not collect any more data or samples on you for the purpose of the study. Data and samples collected up until the time that you withdraw may be retained and used in order for the study to be scientifically valid. Data and samples sent to the NIDDK Repository will be given a unique code number and identifiable information will be removed. Data and samples that have been stripped of personal identifiers cannot be retrieved. You may send this written notice to the following address:

Dr. Peter Reese
917 Blockley Hall
423 Guardian Drive
Philadelphia, PA 19104-6021

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study. You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document, you are permitting the University of Pennsylvania Health System and UPenn School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigators listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns, or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

______________________________	____________________________	_________
Printed Name of Subject	Signature of Subject	Date
______________________________	____________________________	_________
Printed Name of Person Obtaining Consent	Signature	Date

If you agree to participate in this study, you may also agree to let us collect a small biopsy of the donor kidney at the time that the donor's kidney is removed or around the time it is placed in you. The sample will be analyzed for this study and for future research studies. If you do not consent to a kidney biopsy for this research study, your doctor may still collect a biopsy as part of your standard healthcare. You may also agree to the use of any additional biopsies collected "for cause" (i.e., because your doctor thinks it's required for your care) or due to your center's usual program of post-transplant care.

> Are you willing to allow the study team to collect or obtain from your standard healthcare a biopsy of the donor kidney <u>collected around the time of transplant</u> for use in analyses and future research studies?
>
> ☐ Yes ☐ No
>
> Are you willing to allow the study team to store kidney biopsy samples <u>collected "for cause"</u> for use in analyses and future research studies?
>
> ☐ Yes ☐ No

Printed Name of Subject	Signature of Subject	Date
Printed Name of Person Obtaining Consent	Signature	Date

If you agree to participate in this study, you may also agree to let us store your samples (biospecimens) for future research. These stored samples may help us learn more about hepatitis C and transplant. We will label your stored samples with a code that only the study team can link to you. We will keep any information that can be traced back to you as private as possible. If you change your mind and decide you do not want us to store your samples, please contact us. We will do our best to comply with your request, but cannot guarantee that we will always be able to destroy all your samples. Data and samples that have been stripped of personal identifiers cannot be retrieved.

We might send your samples to other investigators for their research, without any information that can identify you. We might also share information such as your sex, age, health history, or ethnicity. We will not sell your samples and you will not be paid for any products that result from the research. Some future studies may need health information (such as smoking history or present health status) that we don't already have. If so, our study team will contact you. Future research that uses your samples will probably not help you, but it may help us learn more about how to treat or prevent hepatitis C and other health problems related to transplant. In general, the research tests we perform are not like routine medical tests, and may not relate directly to your medical care.

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

Are you willing to allow the study team to take and store a sample of your blood and urine for future genetic testing or other research testing?

☐ Yes ☐ No

Are you willing to allow the study team to share your blood and urine samples with other research teams to learn about hepatitis C virus? The blood samples, if shared, would not be labelled with your personal information.

☐ Yes ☐ No

______________________________	____________________________	_________
Printed Name of Subject	Signature of Subject	Date
______________________________	____________________________	_________
Printed Name of Person Obtaining Consent	Signature	Date