Protocol Title: Real World Administration of Zepatier (Grazoprevir plus Elbasvir) in Chronic Hemodialysis Patients with Hepatitis C Infection. Strategies for Identification of Candidate Hemodialysis Patients, Obtainment of Insurance Approval, Treatment Guidelines, and Laboratory and Clinical Monitoring During Therapy Directed to Nephrologists

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UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	"Real World" Administration of Zepatier (Grazoprevir plus Elbasvir in Chronic Hemodialysis Patients with Hepatitis C Infection. Strategies for Identification of Candidate Hemodialysis Patients, Obtainment of Insurance Approval, Treatment Guidelines, and Laboratory and Clinical Monitoring During Therapy Directed to Nephrologists
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Why am I being asked to volunteer?

You are being invited to participate in a research study because you are a hemodialysis patient and your blood tests indicate you have Hepatitis C infection. This study is offering you treatment for Hepatitis C with a drug Zepatier.

Your participation is voluntary which means you can choose whether or not you want to participate. The research team is going to talk to you about the research study, and they will give you this consent form to read. 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 investigator and/or the research team about this form. If you decide to participate, you will be asked to sign this form and you will be provided a copy of this form. Your doctor may be

an investigator in this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

What is the purpose of this research study?

The purpose of this study is to learn if dialysis doctors can treat dialysis patients infected with Hepatitis C themselves.

Hepatitis C infection is common in hemodialysis patients. There are new medications, such as Zepatier, which can cure hepatitis C in > 95% of patients. Zepatier is particularly good for hemodialysis patients with Hepatitis C since the drug is eliminated by the liver and not the kidney. Zepatier is currently approved by the Food and Drug Administration (FDA) to treat certain types of hepatitis C in dialysis patients. For most patients with hepatitis C, one pill per day of Zepatier for 12 weeks will be sufficient. However, there may be so patients who may require 16 weeks of therapy or the addition of another FDA approved drug called Ribavirin. If you need 16 weeks of treatment or the addition of Ribavirin you will be told at the screening visit.

Routine testing of all the patients in your dialysis unit, has identified patients such as yourself, with blood studies that demonstrate a hepatitis C infection. If you choose to participate in this study, other testing will be done to see if you qualify. If you do qualify, you will be provided medication for treatment of your hepatitis C at no cost.

How long will I be in the study?

You will be in the study for 24 to 28 weeks: 12 weeks of pre-screening, 12 to 16 weeks of taking the medication, and then 12 weeks of follow up, after which we will obtain blood tests to show if your hepatitis C infection has been cured.

Expected total duration of the study?

The expected duration of the study for all patients is approximately one year.

What am I being asked to do?

As a participant in this study, you will be asked to take medications which are FDA approved to treat Hepatitis C in hemodialysis patients. Before starting the medications, you will have blood tests performed and a scan of your liver. Once you start the medications you will get additional laboratory testing every 4 weeks. A Hepatitis C viral load will be checked 12 weeks after your last dose of

medication. All of the testing is routine and standard for patients taking medication to eradicate hepatitis C

The following are a list of tests which you will need to do as a participant in this study:

1. **Hepatitis C Genotype** – There are several different strains of the hepatitis C virus and this blood test will tell us which strain you have. Our medication treatment of your hepatitis C will be tailored to your type of hepatitis C. You will have this test only once

2. **Hepatitis C Viral Load** – this blood test will tell how much of the hepatitis C virus is in your body and we use this test to see how well the treatment is working.
   We expect that with treatment the number of hepatitis C viruses in your body will decrease and eventually disappear. We do this test before starting medication, every 4 weeks while on medication, and then 12 weeks after stopping medication

3. **Hepatitis B Surface Antigen and Hepatitis B Core Antibody** – these tests will tell us if you have an infection with Hepatitis B as well as Hepatitis C. It is important to know this since medication used to treat hepatitis C can sometimes make hepatitis B infections worse. This blood test is done only once prior to starting your hepatitis C treatment

4. **HIV antibody** – This test will tell us if you have an infection with HIV. This is important since medications used to treat HIV infection may have to be changed due to interactions with the medications used to treat Hepatitis C. If you do have HIV, we will work with your HIV doctor to make sure you are on the correct medications. This blood test is done only once before starting your hepatitis C medications

5. **Protime and Partial Thromboplastin Time** – These tests tell us if your blood has a problem clotting. We do these tests to make sure your liver is healthy enough to make the proteins needed for these tests to be normal. These tests are performed only once prior to starting your hepatitis C medications . If you are receiving warfarin during the administration of Zepatier, your protime and INR will be checked on a weekly basis to detect any fluctuations in the INR caused by Zepatier on the effect of warfarin

6. **Liver Function Tests** – these blood tests tell us about the health of your liver. We do these just before starting your medication and then every 4 weeks while on medication to make sure your liver health does not change during treatment

7. **Fibroscan** – This is an ultrasound of your liver and is done only once before starting treatment. An ultrasound is a test where a small microphone is placed on the skin over your liver and takes a picture of your liver. The test has no discomfort, no risks, and takes about 10 minutes

It is important to note that none of the blood tests or the ultrasound of your liver are experimental. These are all standard tests that are done in all patients getting treated for hepatitis C

What are the possible risks or discomforts?

Risks of Zepatier – common side effects include: headache, fatigue, nausea, vomiting, yellowing of skin or eyes, change in stool color, insomnia, and diarrhea.

During clinical trials with Zepatier, about 1% of patients developed worsening of their liver enzyme tests and most had no symptoms. These abnormal liver enzymes went away despite continued treatment with Zepatier or after Zepatier treatment was completed.

People being treated for Hepatitis C with Zepatier or similar medications can have an increase in Hepatitis B levels in their blood if they also have that infection. Although this side effect was rare, we will monitor Hepatitis B levels in your blood if you have evidence of past Hepatitis B infection.

If you are receiving warfarin during the period Zepatier is being given, it is possible that Zepatier can interact with your warfarin and cause a fluctuation in your Protime and INR. In patients on warfarin, Protime and INR will be measured weekly during this study to look for fluctuations which will result in dosage adjustments of your warfarin.

The risk of being treated with Zepatier by a Nephrologist (kidney specialist) will be minimized by having a Hepatologist (liver doctor) who is experienced in using drugs like Zepatier, as part of the research team for this study. Prior to your participation, the study liver doctor will review your records to assure that you meet all the inclusion criteria and have none of the exclusion criteria. If during this review of your records, the liver doctor deems it necessary, you will be evaluated in person before or after study participation by the liver doctor

Risks of Ribavirin – In some participants, it may be necessary to add a second drug called Ribavirin to Zepatier to achieve cure. Participants who will need Ribavirin include: those with resistance to Zepatier, have failed treatment for hepatitis C in the past, or have a type of hepatitis C genotype 4.

Ribavirin can cause the hemoglobin level, which is a measure of the number of red blood cells in the body, to decrease. We will give Ribavirin at a reduced dose

to minimize the risk of this complication. We also check your hemoglobin every week during the study; as a dialysis patient weekly hemoglobin levels are routine. A decrease in hemoglobin from Ribavirin use is usually mild and will resolve when the Ribavirin is stopped. Other side effects of Ribavirin include: fatigue, headache, insomnia, depression, dizziness, hair loss, rash, itchiness, sweating, nausea, vomiting, diarrhea, abdominal pain, change in liver function tests, low white blood cells, low platelets, muscle pain, joint pain, flu-like symptoms, shortness of breath, cough, or fever.

Risks, Discomforts, and Inconveniences of Study Procedures – None of the blood tests or ultrasound test pose any health risk to you. We will obtain blood tests during your dialysis treatment to minimizediscomfort and inconvenience. We may ask you to have your labs done at the Laboratory Testing area of Penn Presbyterian Medical Center. In this case, there will be a minor discomfort with the needle stick and a minor inconvenience with going to the lab. For the liver ultrasound you will go to different building on the Presbyterian Hospital campus to have this test done – this will be arranged with you by an appointment which is convenient for you

Illness During Study – If at any time during the study you develop a medical problem you should tell the doctor who you see for this problem that you are in a study for treatment of Hepatitis C

Reproductive Potential

No women of reproductive potential can enroll in this study. We will consider 12 months of no menstrual periods to meet this requirement. Ribavirin may cause birth defects and/or death of the exposed fetus and prior to starting Ribavirin, you will have a pregnancy test. If you are a male, you should not take this drug if your female partner is pregnant.

Unforeseen Risks – Although Zepatier and Ribavirin have been extensively tested and the risks associated with these drugs has been described earlier in this consent form, the investigators want you to know that both of these drugs may have risks which are unforeseen and not described in this document. You are to immediately report any medical symptoms or problems to your dialysis doctor while on these drugs.

Reproductive risks: Because of the effects of Zepatier and Ribavirin, there could be serious harm to unborn children or children who are breast-feeding. For women, if you are currently pregnant, you must inform the research doctor and you will not be allowed to participate in this study. If you are able to become pregnant, you need to inform the research doctor since you will not be able to participate in this study. If you do become pregnant during this study, you must tell the research doctor and consult an obstetrician or maternal-fetal specialist. For men, you and/or your partner are asked to use a medically

accepted method of birth control (such as condoms or oral contraceptives) while you participate in the study.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

The primary benefit of being in this study is that you will be treated for your Hepatitis C infection with Zepatier at no cost to you. There is a >95% chance your Hepatitis C will be cured. However, it is possible you will not be cured and may not get any benefit from being in this research study.

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

If you chose not to participate in this study, you may still be eligible to have your Hepatitis C infection treated if you meet standard medical criteria for treatment, should you choose to do so. There are several other alternative treatments that may be available to you. You may be eligible to get Zepatier or other similar drugs approved to eradicate Hepatitis C from your primary care physician or a specialist in Infectious Disease or Liver disease. You may also chose not to be treated for your Hepatitis C but you should be aware that not being treated for Hepatitis C can put you at risk for cirrhosis and liver cancer. If you decide not to have treatment for Hepatitis C, you should discuss this with your primary care physician. All alternative treatments can be discussed with your primary care physician.

Will I be paid for being in this study?

There is no monetary compensation for participation in this study. Merck, the study sponsor, will be provide Zepatier and if needed Ribavirin free of charge.

Will I have to pay for anything?

All of the blood tests and liver ultrasound in this study are considered routine standard of care in patients who undergo treatment for Hepatitis C. As such, your medical insurance should provide coverage of the costs of these tests.

You are still responsible for any deductibles or applicable co-pays for routine office visits, scans and blood work. Merck will cover the expenses of any laboratory testing which is routine and not covered by your health insurance. Please talk to your doctor and study team about putting you in touch with a

financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance

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

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

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

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

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care. If you do decide to leave the study early before completion, it is possible that you will still be infected with Hepatitis C.

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

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific

meetings, your name and other personal information will not be used. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

If you test positive for HIV, by law we have to report the positive test results to the City of Philadelphia Health Department and/or the PA Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease. For more information about the requirements reporting infectious diseases to the PA Health Department, please visit http://www.health.pa.gov/Your-Department-of-Health/Offices%20and%20Bureaus/epidemiology/Pages/Reportable-Diseases.aspx#.V620aZ3D9eU.

The paper medical records of your participation will be kept in secured location. Some or all of your medical records will also be part of the electronic medical record of the University of Pennsylvania Health System which has a variety of policies and other protections to keep these electronic records secure. You should know that the Investigational Review Board of the University of Pennsylvania will have access to your records, if needed. You will be identified by name and medical record number in these paper and electronic records.

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.).

HIPAA AUTHORIZATION

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

- Name, date of birth, medical record number
- Personal and family medical history
- Results from a physical examinations, tests or procedures
- Current and past medications or therapies

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 right
- to evaluate and manage research functions.

Who may use and share information about me?
The following individuals may use or share your information for this research study:

The investigator for the study (Dr. Michael Rudnick) and the study team

Other authorized personnel at Penn

Who, outside of the School of Medicine, might receive my information?

Oversight organizations

The Food and Drug Administration

The Office of Human Research Protections

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator 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.

How long may the 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 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 University of Pennsylvania's Institutional Review Board grants permission

As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

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 School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

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 Investigator 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.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date

(Optional) Use the authorization line only in studies which are approved by the IRB to use representatives to authorize a subject's participation in research. Delete if not applicable.

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

Authorized subject representative **[print]**	Authorized subject representative Signature	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.