DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Lung Transplantation in Chronic HCV Infection with Post Transplant EPCLUSA Treatment: A Pilot Feasibility and Efficacy Study

CONCISE SUMMARY

The purpose of this study is to evaluate whether treatment with the direct acting antiviral (DAA) Epclusa (sofosbuvir/velpatasvir) after lung transplantation in individuals with chronic hepatitis C infection is feasible, safe and effective at curing HCV..

This study involves a screening visit prior to your lung transplant. It also involves an HCV treatment screening visit, an HCV treatment initiation visit that may be combined with the HCV treatment screening visit, and follow-up visits at week 4, week 8, week 12, week 24, and week 48. You will be treated with Epclusa for 12 weeks. Participants will be asked to provide blood samples for testing and will undergo tests, exams, and procedures for study purposes.

There are risks associated with Epclusa. Some risks include: headache, fatigue, nausea, asthenia, and insomnia.

If you are interested in learning more about this study please continue reading.

You are being asked to take part in this research study because you have Hepatitis C (HCV) and are being considered for lung transplant. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

Dr. Omar Mohamedaly will conduct the study and it is funded by Gilead Sciences. This is an investigator sponsored study that was initiated by Dr. Mohamedaly. Gilead Sciences will pay Duke University to perform this research, and these funds may reimburse part of Dr. Mohamedaly's salary.

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, Dr. Mohamedaly will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?
Chronic active hepatitis C is currently considered a contraindication to lung transplant at most lung transplant centers, including Duke. However, in recent years, a new class of medications, called direct

acting antiviral (DAA) therapies have been approved by the U.S. Food and Drug Administration (FDA) and been proven to be highly effective at curing hepatitis C infection. There have been no formal clinical studies evaluating whether those with end stage lung disease and hepatitis C can safely undergo lung transplant and then treated and cured of the hepatitis C infection after transplant using a DAA regimen.

The purpose of this study is to evaluate whether treatment with the direct acting antiviral (DAA) Epclusa (sofosbuvir/velpatasvir) after lung transplantation in individuals with chronic hepatitis C infection is feasible, safe and effective at curing HCV. Epclusa is approved by the FDA for the treatment of chronic Hepatitis C (HCV) infection.

The current standard of care at Duke is not to transplant lungs from donors with known active hepatitis C or to perform lung transplant in recipients with chronic hepatitis C infection. Utilizing organs from hepatitis C donors into hepatitis C recipients is commonly done in abdominal transplant throughout the United States. Data suggest this can result in shorter average wait times without other significant adverse results. In this study, organ donors will be considered regardless of their hepatitis C status. This will allow the surgeons to evaluate more donors to find high quality lungs that are a good match for you. Other than donor HCV status, all lungs used for transplant will meet our standard criteria for donor lungs. You will be transplanted using the first appropriate lungs for which you are eligible based on the national waitlist and organ allocation system.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 10 people will take part in this study at Duke.

WHAT IS INVOLVED IN THE STUDY?
If you agree to be in this study, you will be asked to sign and date this consent form.

<u>Screening Visit (this visit occurs before your lung transplant)</u>
The following data will be collected from your medical chart:

- Medical and medication history
- Liver biopsy results
- Transient Elastography (FibroScan) results – This is a non-invasive test that measures liver stiffness.
- Laboratory results
- EKG results

<u>HCV Treatment Screening Visit</u>

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Once you have recovered from your lung transplant, have been discharged from hospital, and are well enough to begin therapy in the opinion of your transplant physician and study doctor, you will be referred for the treatment screening visit.

The following tests and procedures will be done at this visit:

- A pregnancy test will be done on child bearing potential women (approximately ½ teaspoon/3 mls).
- A blood sample will be collected for HCV status (approximately 1½ teaspoons/8 mls).
- EKG
- If you are eligible to start Epclusa treatment a 6 week supply will be dispensed. You will be provided with a diary to keep track of when you take Epclusa.
- Your medication list will be reviewed.
- Clinical data related to transplant and donor will be collected from your medical chart.

HCV Treatment Initiation Visit
You will be started on EPCLUSA treatment. Treatment consists of 1 pill taken by mouth once a day, either with or without food. Treatment will last 12 weeks. This visit can be combined with the treatment screening visit if you are eligible at that time.

- 6 weeks of Epclusa treatment will be dispensed for you to take at home.

Week 4
The following will be done at this visit:

- Dispense 6 weeks supply of Epclusa.
- Your study drug diary will be reviewed.
- You will meet with the study coordinator to review medications, side effects and changes in your health.

Week 8
The following will be done at this visit:

- You will meet with the study coordinator to review medications, side effects and changes in your health.
- Your study drug diary will be reviewed.

Week 12
The following test and procedures will be done at this visit:

- A blood sample will be collected for HCV status (approximately ½ teaspoon/3 mls).
- Your study drug diary will be reviewed.

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- You will meet with the study coordinator to review medications, side effects and changes in your health.

Week 24
The following test and procedures will be done at this visit:

- A blood sample will be collected for HCV status (approximately ½ teaspoon/3 mls).
- You will meet with the study coordinator to review medications, side effects and changes in your health.

Week 48
The following test and procedures will be done at this visit:

- A blood sample will be collected for HCV status (approximately ½ teaspoon/3 mls).
- You will meet with the study coordinator to review medications, side effects and changes in your health.
- Transient Elastography (FibroScan). This is a non-invasive test to measure liver stiffness.

The total amount of blood taken from you throughout the entire study for research purposes only is approximately 20 mls (4 teaspoons).

HOW LONG WILL I BE IN THIS STUDY?
Your participation in this study will be approximately 1 year. You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

WHAT ARE THE RISKS OF THE STUDY?
As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

What are the risks of lung transplantation with HCV?
The risks of lung transplantation in individuals with hepatitis C does not appear to be significantly different from those without hepatitis C. A review of the U.S. national experience comparing outcomes between lung transplant recipients who were HCV antibody positive and those who were HCV antibody negative between 2000-2011 did not reveal a difference in median survival.

Risks of Epclusa
Common (10% or above)

- **Headache**
- **Fatigue**

- Slow heart rate (bradycardia) may occur if Epclusa is taken with amiodarone, a medicine used to treat certain heart conditions.

Less common (5% to 9%)

- **Nausea**
- **Asthenia (weakness, lack of energy)**
- **Insomnia (difficulty sleeping)**

Hepatitis B virus reactivation: f you have ever had hepatitis B, the hepatitis B virus could become active again during and after treatment with EPCLUSA. You will have been assessed for hepatitis B as part of your lung transplant evaluation. If this testing showed evidence of hepatitis B infection, you will not be able to participate in this study.

Risks of Drawing Blood

Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Risks of ECG

Possible side effects of the ECG are skin irritation, itching and redness from the ECG electrode pads.

Risks of Reproductive Potential

Female

Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can continue in this study. If sexually active, you must agree to use appropriate contraceptive measures for the duration of the study. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. If you do become pregnant during this study or if you have unprotected sex, you must inform your study physician immediately.

Drug and Food Interactions:

For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

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There may be risks, discomforts, drug interactions or side effects that are not yet known.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
Instead of being in this study, you could choose to be treated for hepatitis C prior to lung transplant evaluation. You also could seek out consideration by other lung transplant programs. Most programs in the United States have historically turned down candidates with active hepatitis C, however the Cleveland Clinic has transplanted patients with hepatitis C in the past. Every lung transplant program has its own criteria for transplant listing which may change over time.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there may be direct medical benefit to you. Duke is currently not transplanting individuals with chronic hepatitis C infection outside of this protocol, so participating in this study will make you eligible to be considered as a candidate for a lung transplant. The suitability for transplant is ultimately made by the Lung Transplant Team, and dependent on multiple factors. Agreeing to participate in this study is not a guarantee for transplant. Participating in this study will make you eligible to receive lungs from a donor with known HCV which may result in a shorter wait time. Previous studies have demonstrated that clearance of HCV virus is associated with decreased rates of death and cirrhosis, although this cannot be guaranteed. We hope that in the future the information learned from this study will benefit other people with your condition.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, Dr. Mohamedaly and his study team will report the results of your study-related laboratory tests and procedures to Gilead. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, representatives of Gilead and designees, and the Duke University Health System Institutional Review Board. If any of these groups review your research record, they may also need to review your entire medical record.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

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This information may be further disclosed by the sponsor of this study. If disclosed by the sponsor, the information is no longer covered by federal privacy regulations. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your identity will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information

WHAT ARE THE COSTS TO YOU?
You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all services are covered by insurance. Some procedures or scans may require pre-authorization by your insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the study with the study team. At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

Gilead will provide the study drug free of charge to you. At the end of the study, or if you decide to withdraw from the study before it ends, you may be asked to return all unused study drug. Your study doctor may request that you return for a checkup before you stop your study drug if she thinks that stopping it suddenly may harm you and may ask you to complete the tests that would ordinarily occur when a person completes the study.

WHAT ABOUT COMPENSATION?
There is no compensation for participation in this study.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary

compensation or free medical care to you in the event of a study-related injury. The drug manufacturer, Gilead Sciences, Inc.will reimburse for the costs of medical care you receive foran illness or injury resulting solely from a defect in the study drug, Epclusa®, provided all aspects of the study protocol have been followed correctly.

For questions about the study or research-related injury, contact Dr. Mohamedaly at (919) 684-6140 during regular business hours. After hours and on weekends and holidays please call the Duke Hospital operator at (919) 684-8111 and ask to have Dr. Mohamedaly paged.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Mohamedaly in writing and let her know that you are withdrawing from the study. His mailing address is DUMC 102361, Durham, NC 27710.

Dr. Mohamedaly may ask you to return for a checkup before you stop your study drug if he thinks that stopping the drug suddenly may harm you. He may also ask you to complete the tests that would ordinarily occur when a person completes the study.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study medication if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. If this occurs, you will be notified and your study doctor will discuss other options with you.

If you agree to allow your blood samples to be kept for future research, you are free to change your mind at any time. We ask that you contact Dr. Mohamedaly in writing and let him know you are withdrawing your permission for your blood samples to be used for future research. His mailing address is DUMC 102361, Durham, NC 27710. At that time we will ask you to indicate in writing if you want

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the unused blood samples destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

A description of this clinical trial will be available on https://www.clinicaltrials.gov/ct2/home 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.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Mohamedaly at (919) 684-6140 during regular business hours. After hours and on weekends and holidays please call the Duke Hospital operator at (919) 684-8111 and ask to have Dr. Mohamedaly paged.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

STATEMENT OF CONSENT
The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form.

_____ _____ _____
Signature of Subject Date Time

_____
Printed Name of Subject

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____
Printed Name of Person Obtaining Consent