Informed Consent for patients: Sponsor-Investigator Initiated CRI #15-05

Title: Bridging Care to HCV Treatment Among Opioid Dependent Patients on Buprenorphine/naloxone Maintenance Therapy: A Pilot Study of Treating HCV with Epclusa at a Psychiatrist-staffed Outpatient Addiction Clinic

Approved: August 3, 2017

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INFORMED CONSENT

TITLE:	Bridging Care to HCV Treatment Among Opiate Dependent Patients on Buprenorphine/naloxone Maintenance Therapy: A Pilot Study of Treating HCV with Epclusa at a Psychiatrist-staffed Outpatient Addiction Clinic
PROTOCOL NO.:	15-05 WIRB® Protocol #20170423
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FUNDER:	Gilead
SPONSOR:	Community Research Initiative of New England
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SITE(S):	Outpatient Addiction Services Cambridge Health Alliance 26 Central Street Somerville, MA 02143 United States Tel: 617-665-1000 Email: zschuman@challiance.org
STUDY-RELATED PHONE NUMBER(S):	Amy Colson, MD, MPH 617-502-1700 617-502-1799 (24-hours)
SUB-INVESTIGATOR(S):	Zev Schuman-Olivier, MD

INTRODUCTION

You are being asked to take part in a clinical research study involving a currently available treatment for Hepatitis C virus (HCV). The treatment, Epclusa, is approved by the Food and Drug Administration for treatment of HCV. It is a fixed-dose combination (FDC) tablet which combines two separate medicines called sofosbuvir (SOF) and velpatasvir (VEL) into one tablet for the treatment of the Hepatitis C virus (HCV). This consent form gives you information about the study. A member of the study staff will read through the consent with you, discuss all the information, and will answer any questions that you may have. Ask your study doctor or study nurse to explain any words or information in this consent form you do not clearly understand. You should understand the purpose of the study, how taking part may help you, any potential risks to you, and what is expected of you during the study. If you then want to be in the study, you will be asked to sign this consent form. Once signed, you will receive the signed and dated copy to keep.

You may show this consent form to family, other doctors, or friends. You may want to discuss it with them to help you decide if you want to be in this study. If you don't know another doctor but want a second opinion about this study, please ask. The study doctor will recommend someone for more information.

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.

WHAT IS THE PURPOSE OF THIS STUDY?

The main purpose of this study is to assess the safety and effectiveness and tolerability of Epclusa in HCV-treatment naïve and treatment-experienced (including treatment-intolerant) subjects with chronic HCV infection who regularly attend a clinic for Suboxone therapy.

Epclusa is an FDA approved drug that is used to treat chronic Hepatitis C Infection. In clinical trials of Epclusa, medication side effects were generally mild. The most common side effects seen were tiredness and headache. Nausea, lack of energy and insomnia were also seen in clinical trials of Epclusa in a small fraction of participants (less than 10%).

Epclusa has been shown to be effective in curing Hepatitis C infection. In clinical trials, cure rates ranged from 89% to 98% depending upon patient characteristics and duration of treatment.

You are being asked to be in this study because you:

- Are infected with the Hepatitis C virus
- Meet safety criteria for treatment with Epclusa

Dr. Amy Colson is the person in charge of this study at Community Research Initiative. She will work with nurses and doctors at Cambridge Health Alliance to conduct the study. Your study visits will take place during your regularly scheduled visits to the Suboxone clinic. Epclusa will be provided to you at no charge.

This Informed Consent refers to the Community Research Initiative staff as the "study staff" and to the doctor that you regularly see for your medical care at the Suboxone clinic as your "study doctor." The doctor who oversees this study is referred to as the "Principal Investigator."

HOW LONG WILL THIS STUDY LAST?

The study is expected to last for 48 weeks. Twenty individuals with HCV at one clinic in the United States will be enrolled in this study.

THE STUDY:

If it is determined that you are eligible for the study, you will be provided treatment with Epclusa for the full treatment course of 12 weeks as prescribed by your study doctor.

WHAT ARE THE PROCEDURES OF THIS STUDY?

<u>Screening Visit</u>

The first visit of the study is the screening visit to see if you qualify for the study. At this visit, the study staff will go over this consent form with you. If you want to be in the study, you will sign this consent. At this visit, after you sign the consent, you will be asked about:

- Your recent medical history including recent or past drug allergies
- Your current medical health
- The medications that you take
- your current alcohol use

In addition, the following may occur:

- Blood samples (between 1 and 2 tablespoons) will be obtained to evaluate:
  - HCV viral load (amount of HCV in your blood)
  - HCV genotype test (to determine the type of HCV infection, if not yet known)
  - Complete blood panel
  - Hepatic function tests ALT, AST (test the function of your liver)
  - Basic metabolic panel and estimated GFR (tests of your kidney function)
  - FibroSure (to estimate the amount of fibrosis of your liver)

  - Hepatitis B virus testing to assess for presence of active infection or immunity to the virus
  - Serum pregnancy test if you are a woman who can become pregnant
- Urine sample for drug screening and presence of Suboxone
- Vital signs including blood pressure, pulse, height and weight
- A recording of the rhythm and speed of your heartbeat

These test results will be used to see if you qualify for this study.

Baseline Visit

This visit will occur within 30 days of the screening visit during a regularly scheduled clinic visit. At this visit you will do the following:

- Complete three questionnaires about your health and quality of life
- Supply a urine sample for drug screening and presence of Suboxone
- Have a urine pregnancy test if you are a woman who can have children

In addition, at this visit the study doctor and study staff will do the following:

- Review all medicines that you are taking
- Review side effects and new physical findings that you may have
- Measure your blood pressure, pulse, and weight
- Perform a physical examination if indicated
- Provide Epclusa study treatment
- Provide medication adherence counseling

Every two weeks during your study treatment you will be seen during a regular OAS clinic visit:

At each visit during treatment with Epclusa the study staff and doctor will do the following:

- Review all medicines that you are taking
- Review side effects and new physical findings that you may have
- Measure your blood pressure, pulse, and weight
- Review medication adherence and provide adherence counseling
- Provide study medications
- Collect study medication containers

At each visit the following will also occur:

- Supply a urine sample for drug screening and presence of Suboxone
- Have a urine pregnancy test if you are a woman who can have children

At the Week 4 visit only:

- Blood samples (between 1 and 2 tablespoons) will be obtained to evaluate:
  - HCV viral load (amount of HCV in your blood),
  - Hepatitis B virus testing to assess for presence of active infection
  - Hepatic function tests ALT, AST (test the function of your liver)
- Complete three questionnaires about your health and quality of life

At your final treatment visit only study staff will ask you to do the following:

- Complete three questionnaires about your health and quality of life

Post-Treatment Assessments

After you have completed your Epclusa study treatment, you will be seen at the clinic for study visits. These visits will take place 4 weeks and 12 weeks after your stop Epclusa treatment. At this visit study staff and the study doctor will:

- Review all medicines that you are taking
- Review side effects and new physical findings that you may have

In addition:

- a blood sample will be drawn to assess HCV viral load (amount of HCV in your blood)

At the post-treatment week 12 visit only:

- Complete three questionnaires about your health and quality of life

Instructions for Taking Study Medication

The study medication is formulated as a tablet and should be stored at room temperature. Take one tablet by mouth daily, with or without food.

Tablets will be supplied in bottles with 28 doses in each bottle. When you are given your study medication bottle by study staff, you will also be given a bottle cap that has an electronic dose recording system embedded in the packaging. It is very important that you return the entire bottle and cap to the study doctor at each visit during treatment. The study doctor or study staff will download your dosing information from the packaging at every visit and review it with you.

Subject's Responsibilities

As a participant in this study, it is your responsibility:

- to come to the study site for all scheduled study visits
- to take the medications according to the directions given by the study doctor and study staff
- to return your study medication packaging at each study visit
- to tell study staff about all medications you are taking
- to tell study staff about any side effects you may have

ARE THERE MEDICATIONS THAT YOU CANNOT TAKE WHILE ON THIS STUDY?

We encourage you to discuss all medications and herbal supplements you plan to take during the study, including:

- Any prescription drugs, including vaccines
- Any over the counter medicines
- Any herbal preparations

At each visit the study staff will review all medicines you are taking. You should call the study staff any time you are given a new medicine prescribed by another doctor. You will be given the staff number and a pager number.

WHAT PROCEDURES ARE BEING PERFORMED FOR THE PURPOSES OF THIS STUDY (THAT ARE NOT CONSIDERED STANDARD CARE FOR YOUR HCV INFECTION)?

- More frequent medical monitoring
- Pregnancy tests
- Responding to questionnaires
- Electronic recording of dosing by study medication packaging

WHAT ARE THE RISKS AND DISCOMFORTS?

RISKS AND BENEFITS

Epclusa:

There are potential side effects associated with the use of Epclusa including tiredness, headache, nausea, lack of energy and insomnia. In clinical trials, these side effects were generally mild and were seen in less than 25% of participants.

Blood Draws

In addition to risks associated with the study drug, drawing blood from a vein may cause local pain, bruising, occasional lightheadedness, fainting, and very rarely, infection at the site of the blood draw.

Other Risks:

As with any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reaction are rash; difficulty breathing; wheezing; sudden drop in blood pressure; swelling around the mouth, throat or eyes; a fast pulse; and sweating.

Please seek treatment and inform the study doctor and study staff at once if you have any of these symptoms, or any other side effects, during the study.

There is a possibility that Epclusa will not treat your HCV. Epclusa is generally effective but has reduced effectiveness when not taken correctly. It is very important to follow the study doctor and study staff's dosing instructions.

You may have side effects that are not yet known or have not yet been reported.

If you want to be in this study, you may be excluded from participating in other studies at the same time. If you are taking part in another study, you should let the study staff know about the other study. The study staff person will need to make contact with the other study site to make sure that it is all right for you to also participate in this study. The study staff person will also need to discuss this with the study medical monitor to make sure that participation in both studies is allowed.

Possible Benefits of the Study

There is no guarantee that you will receive personal benefit from participating in this study. Your participation in this study may benefit the community, scientists and doctors who work with HCV by providing increased knowledge and information about the treatment of your disease.

PREGNANCY AND BREAST FEEDING

WHAT IF YOU ARE CONSIDERING HAVING A CHILD?

Women:

The safety of Epclusa has not been studied in pregnant women. If you are a woman who can become pregnant, you can only be in this study if you are not pregnant and use birth control that is very reliable for the duration of the study and until at least 8 weeks after the last dose of

study medication. A barrier type of birth control is required in addition to the use of an IUD, hormonal contraceptive or a second barrier method. Barrier methods include male condoms (should be used without spermicide), female condoms, diaphragms, and cervical caps. This would not be required if you are non-heterosexually active, practice sexual abstinence, or have a vasectomized partner (confirmed sterile) or have undergone a tubal ligation (tubes tied). Pregnancy tests will be done before you start on the study, at each study visit, and at any time that pregnancy is suspected. It is important for you to tell the study doctor at once if you get pregnant or think that you might be pregnant while you are in the research study. If you become pregnant while on the study, you will be discontinued from the study. You may also be asked questions about your pregnancy and the baby. Your study doctor will want follow up information on your infant for a minimum of 8 weeks.

Breast-feeding:

Medicine can pass from mother to a nursing child. This may cause harmful side effects to the child. The safety of Epclusa for the nursing baby is not known. Women who are breast-feeding may not be in this study.

Men:

The effect of the study drugs on sperm is not known. You should not father a child or donate sperm while you are on the study and for 90 days after receiving the study drug. If you have sex with a woman who can get pregnant, you should use a condom. When using a condom, it is recommended to use a condom without spermicide. You must inform your study doctor if your partner becomes pregnant during the study or within 90 days after the last study drug administration.

IF YOU DO NOT PARTICIPATE IN THIS STUDY, WHAT ARE YOUR ALTERNATIVES FOR CARE?

Instead of being in this study, you may be eligible for HCV treatment, including the use of Epclusa, as prescribed by a local HCV treatment specialist.

WILL YOU BE INFORMED OF NEW FINDINGS?

Any new information that is learned about the study drug while you are on the study will be given to you. This new information might cause you to change your mind about staying in the study. You will be asked to sign a new consent form with the new information. This is to show that you have been told about this new information.

HOW WILL YOUR CONFIDENTIALITY BE PROTECTED?

You have a right to privacy. All information collected during this study is confidential as far as the law allows. The study forms (Case Report Forms) record all the information collected during the study. None of these papers will identify you. Your identity will stay confidential.

However, in order to be sure the research is legitimate and legal, auditors and monitors will have access to your study records. These people are there to make sure we are doing what we say we are doing. Government authorities such as the Food and Drug Administration (FDA) also need to know that we do indeed have the subjects we say we do. The Western Institutional Review Board (WIRB) may know your name if necessary. That board reviews clinical research studies and is there to protect your interests. Community Research Initiative or someone we hire will look at all of the information gathered from all of your visits. They will use this information to decide whether the study drug was safe for you and the other people in the study.

Information about your participation on this study may be looked at in any country in the world. Community Research Initiative may send the information to health authorities all over the world. The results of the study might be used in reports and scientific meetings or publications. If you leave the study at any time, your information will stay in the study and be used for these reports. *Your identity will never be used.*

Certificate of Confidentiality:

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you.

The Certificate cannot be used to resist a demand for information from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of child abuse and neglect, or harm to self or others.

WILL THERE BE ANY COSTS FOR PARTICIPATING IN THIS STUDY?

You will not pay for the study visits or procedures required by the study that are not a part of standard care for Hepatitis C treatment. You or your insurance company will have to pay for costs of procedures not required by the study. You will also pay for any medical costs for care if your disease becomes worse.

Epclusa will be provided to you. You or your insurance carrier will have to pay for your other medications.

WILL THERE BE COMPENSATION FOR PARTICIPATION IN THIS STUDY?

You will not receive any payment or compensation for your participation in this study.

WILL THE STUDY DOCTOR BE PAID?

Gilead will be providing study drug and funding support to the Principal Investigator at Community Research Initiative and your study doctor to conduct this study. The amount of this payment is sufficient to cover the doctor's and/or institution's expenses to perform the study but provides minimal personal financial benefit to your study doctor.

FINANCIAL DISCLOSURE

The Principal Investigator, Dr. Amy Colson, has received payments from Gilead for attending Scientific Advisory Board meetings. Please feel free to ask any questions you may have about this matter.

Compensation In Case Of Injury:

If you experience any injury or illness as a direct result of your participation in this research study, call Dr. Amy Colson or the study staff at 617-502-1700 or 617-502-1799 (24 hour contact). You will be referred to your Primary Care Physician for immediate treatment. The cost of that treatment will be billed to your insurance company. Your insurance company may not pay. If your insurance company does not pay, or if you do not have an insurance company, you will be responsible for all payments. No funds have been set aside for any other losses such as lost wages, disability, or discomfort relating to injury or illness as a result of your participation in this study.

By signing this consent form, you will not give up any of your legal rights.

CAN YOU WITHDRAW FROM THE STUDY?

Before you can decide if you want to be in this study, it is important that you know that:

- You do not have to be in this study.
- You can decide to stop being in this study at any time.
- Your decision will not result in any penalty or loss of any benefits to which you may be entitled.
- You will be asked to make one last office visit for a final exam and blood work. But, you can refuse to do this.

Removal from study:

You may be removed from the study without your consent for any of the following reasons, or other administrative reasons:

- If the investigator decides staying on the study would be harmful to you
- If you require a treatment not allowed on this study
- If you do not come to the study site for scheduled visits and take your medicine as instructed
- If you become pregnant
- If you have a serious reaction to the study medication
- If the study is canceled by Gilead, Community Research Initiative, the FDA, or Western Institutional Review Board.
- If you become imprisoned or involuntarily incarcerated in a medical facility.

NAMES OF CONTACTS FOR QUESTIONS ABOUT THE STUDY:

Dr. Amy Colson
Staff office: 617-502-1700
Off hours number: 617-502-1799

You should call Dr. Amy Colson or the study staff and study doctor you have been working with for the following reasons:

- If you are worried about how you are feeling
- If you think you may have been hurt because of the study
- If you have questions, concerns, or complaints about the study procedures, medication, etc.

If you have any questions about your rights as a research subject, or if you have questions, concerns, or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, WA 98374-2115
Office: (360) 252-2500
(800) 562-4789
Fax: (360) 252-2498
Email: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

VOLUNTEER'S STATEMENT:

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about being in this study I may contact Dr. Amy Colson, MD, MPH at Community Research Initiative of New England at 617-502-1700.

I understand that my participation in this research project is voluntary. I know that I may quit the study at any time. I may quit without harming my medical care or losing any benefits I might be entitled to. I also understand that the doctor for this study may decide at any time that I should no longer be in this study.

If I have any questions about my rights as a research subject in this study, I may contact:

Western Institutional Review Board (WIRB)
1019 39th Avenue SE, Suite 120
Puyallup, WA 98374-2115
Office: (360) 252-2500
(800) 562-4789
Fax: (360) 252-2498
Email: help@wirb.com

I have read and understand the above information. I agree to be in this study. I have been given a copy of this signed and dated form for my records.

I understand that I do not give up any of my legal rights by signing this consent form.

Study Participant (signature)	Date	Time
Print Participant's Name		
Person who explained this study (signature)	Date	Time
Print Name of Person who explained this study		

The following witness has observed the entire consent process:

Witness Signature (When Appropriate)	Date	Time

Witness's Name (When Appropriate)