CEDARS-SINAI MEDICAL CENTER

CONSENT FORM FOR RESEARCH

TITLE: Pravastatin Intervention to Delay Hepatocellular Carcinoma Recurrence

SPONSOR: NATIONAL INSTITUTE OF HEALTH (NIH)

PRINCIPAL INVESTIGATOR: Shehnaz K. Hussain, PhD, ScM

STUDY CONTACT PHONE NUMBER: Shehnaz K. Hussain, PhD, ScM 310-423-6401

AFTER HOURS CONTACT (24 HOURS): Walid S. Ayoub, MD 310-384-1242

This research study is sponsored by the National Institute of Health (NIH). NIH only reimburses Cedars-Sinai Medical Center (CSMC), Northwestern University (NWU), University of California, Los Angeles (UCLA), Universify of California, San Francisco (UCSF), and Emory University (EU) for the costs associated with running the study; NIH is not providing additional compensation to these institutions or the Investigators for their participation in the study.

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

Hepatocellular Carcinoma (HCC) is a major health concern in the United States, particularly among people with liver cirrhosis. Out of every 100 patients with liver cancer, only 18 will survive 5 years or more. While therapies targeting the liver are used in an effort to combat this disease, there is a high chance of HCC occurring again after these therapies.

Statins are widely used drugs that lower cholesterol levels. Some studies have suggested that statins lower risk of HCC, but this possibility has not been studied thoroughly in a clinical trial.

We are doing this study to examine the effects that pravastatin, a type of statin, has on the time it takes for HCC to occur again in patients with early stage HCC. We think that pravastatin in combination with therapies targeting the liver may delay or protect against HCC occurring again.

You are being asked to take part in this research study because you have been diagnosed with an early stage HCC and have been treated with therapies targeting the liver.

This research study is designed to study the investigational use of pravastatin. Pravastatin is approved by the U.S. Food and Drug Administration (FDA) to lower cholesterol and reduce the risk for heart attack, stroke, and chest pain in patients who have heart disease or at risk for heart disease. However, pravastatin is not approved by the FDA to delay or protect against HCC occurring again.

The study will enroll up to 130 people in total. This study will be conducted and enroll patients at five different sites: CSMC (lead site and data and specimen coordinating center), NWU, UCLA, UCSF, and EU.

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as Appendix A.

The flowchart shows a timeline for research-related or standard of care procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. **Standard of care (routine)** procedures would be performed both as part of this study and if you do not participate in this study.

A table describing common medical procedures done solely for the purposes of monitoring and assessing your condition during this study is attached as Appendix B to the end of this consent form. Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart, attached Appendix A.

Overview of study:

Patients at all three sites will undergo the same research procedures as noted below.

This is a randomized, double-blind research study.

- "**Randomized**" means that you will be assigned to a study group by chance, like flipping a coin. You will be randomized into one of 2 study groups, and will have an equal chance of being placed in one of the groups described above.
- **"Double-blind"** means neither you nor the researchers will know what group you are assigned to.

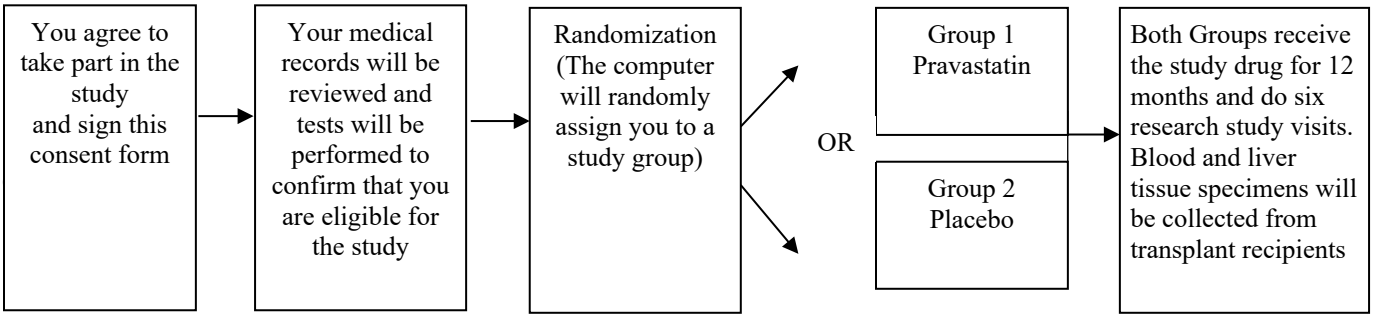
This is a placebo-controlled study. It will compare the effects (good or bad) of pravastatin against the effects of a placebo (an inactive substance, such as, a sugar pill) on the condition being studied in this research.

Research participants in this study will be treated with the study drug, either pravastatin or a placebo. You will not get both. This study has two study groups:

- **Group 1,** the statin group, will receive 40 mg of pravastatin per day in a capsule.
- **Group 2,** the placebo group, will receive a capsule that is identical in color, consistency, and appearance to pravastatin but it will not contain any medication.

A computer will randomly assign you to a study group. This is done because no one knows if the results experienced by the participants in one study group are better, the same, or worse than the results experienced by participants in the other. Once you are put in one group, you cannot switch to another group. Neither you nor your doctor can choose the group in which you will be placed.

Another way to understand what will happen to you during the study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



Data and specimens collected for this study will be stored at the central data and biospecimen repository at CSMC. CSMC will be responsible for storing and maintaining specimens and data from CSMC, UCLA, NWU, UCSF, and EU patients. Specimens collected from patients at UCLA will be packaged in batches and transported via courier on dry ice to CSMC. Specimens collected from NWU, UCSF, and EU will be packaged in batches and shipped overnight on dry ice to CSMC. Data collected from UCLA, NWU, UCSF, and EU will be maintained on a secure CSMC Enterprise Information Systems (EIS) server. Appropriate administrative, physical, and technical safeguards are in place to ensure the confidentiality, integrity, and security of electronic protected health information (EPHI). Security measures for the databases include password management, transmission security, and data encryption to guard against unauthorized access to EPHI while it is being transmitted over the network. Specimens and data will be labeled with a unique code, so identifying information will not be linked to the specimens or data. Only the PIs and study staff from UCLA, NWU, UCSF, and EU will have access to the key code for participants at their institutions.

Coded specimens will be maintained at the central biospecimen repository at CSMC for use in this study. "Coded" means your name and other identifying information will be removed from the specimens, and instead a unique study ID will be linked to the specimen. Your unique study ID and identifying information will be protected and stored separately, so researchers will not be able to easily identify you. Data provided through the questionnaires and medical record review will be maintained in a coded manner on a secured database at CSMC, for the purposes of this research study. Records for patients will only be viewable to research staff from same institution, or members of the Central Quality Office at CSMC for the purposes of eligibility confirmation and monitoring.

Optional Sub-study

You are also invited to participate in a related biological specimen repository in which your specimens and data collected under this study may be used for future research. Details of this repository are described in a separate consent form. You are not required to participate in the repository study in order to take part in this research study.

How long will you be in the study

We think you will be actively participating in this study for about 12 months. The total time includes 6 study visits over 12 months. You will start the study drug (pravastatin or placebo) at the first study visit and will be required to take it daily over these 12 months. Study Visits will take between 1-3 hours to complete. We will make follow-up telephone calls to you 30, 60, and 90 days after completion of Study Visit 6 to assess symptoms and adverse events. If you receive a liver transplant before the end of this study (within or beyond the 12-month intervention period), we will obtain blood

and liver tissue specimens from the liver that is removed at the time of transplantation. No additional visit will be required for these collections.

Regardless of whether or not you receive a liver transplant, we would like to keep track of your medical condition for ten years and review your medical records periodically to see how you are doing. Checking on your condition every so often helps us look at long-term effects of the intervention.

3. WHAT ARE THE POSSIBLE RISKS?

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as Appendix B. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures.

The study drug capsules (pravastatin and placebo) contain a small amount of lactose powder that is much less than the amount of lactose contained in a glass of milk. Mild abdominal issues (cramping, bloating, flatulence, diarrhea, nausea) are possible, but very rare with this small amount of lactose.

Risks of Pravastatin

Pravastatin may affect how different parts of your body work, such as your liver and kidneys. You will have blood tests before and during the study to monitor your organ function. Your study doctor will let you know if changes occur that may affect your health. Women who are pregnant or may become pregnant should not use pravastatin. When taken during pregnancy, pravastatin may cause harm to a developing baby. If you are able to become pregnant, you will have a pregnancy test before the study start. Let your study doctor know immediately if you believe you might be pregnant.

Other possible side effects of pravastatin are summarized in the table below. You will be asked to keep a diary during the study to record any side effects and symptoms you may be experiencing.

Occasional, some may be serious (occurs in 4-20% of people)	**Possible, some may be serious** (occurs in 1-3% of people)	**Rare, and serious** (occurs in less than 1% of people)
• Diarrhea • Musculoskeletal pain (Symptoms: Aching or stiffness of the entire body, twitching muscles, sensation of "burning" in your muscles, localized or widespread pain) • Upper Respiratory Infection (stuffy or runny nose, sneezing, sore throat, or cough)	• Angina Pectoris (uncomfortable pressure, fullness, squeezing or pain in the center of the chest) • Rash • Nausea/vomiting • Muscle Myalgia (pain) • Pharyngitis (Sore throat) • Rhinitis (Stuffy nose) • Cough • Flatulence (gas) • Fatigue	• Confusion, forgetfulness, or memory problems • Dyspepsia/Heartburn • Abdominal Distension (swelling of the abdomen either caused by gas or fluid collection) • Influenza • Dizziness • Allergic reaction including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or

	• Headache	swallowing • Liver failure (symptoms: weakness, fatigue, weight loss, yellowing of the skin or eyes) • Rhabdomyolysis (a breakdown of muscle tissue), a rare condition that may cause kidney damage (symptoms: muscle pain, tenderness, or weakness; dark colored urine)

Food and Medication Interactions
Grapefruit and grapefruit juice may interact with pravastatin and lead to potentially dangerous effects. Do not consume grapefruit products (grapefruit, grapefruit juice, grapefruit seed extract, or dietary supplements containing grapefruit) during the intervention portion of this study.

Pravastatin interacts with many other medications in ways that can increase or decrease the amount of medication in your blood. The interactions could result in increased levels that can be dangerous, or decreased levels so that drugs don't work. Please refer to the attached list of drugs (Appendix C) that must be avoided while you are participating in this study.

Unknown Risks
There also may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they may be serious, long-lasting, permanent, and/or fatal. Tell your study doctor if you notice or feel anything different so they can check if you may be having a side effect.

Alcohol consumption
Pravastatin should be used with caution in patients who consume more than 5 drinks per day of alcohol as pravastatin may cause liver injury. We will monitor your liver function closely.

Reproductive and Lactation Risks
Taking part in this research study can affect an unborn baby. Therefore, you should not become pregnant while on this study. Women who are able to become pregnant will be required to have a pregnancy test before the study, and must agree to use adequate birth control (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation. Let your study doctor know immediately if you believe you might be pregnant.

Women should not breastfeed a baby while on this study.

Unknown Risks to the Developing Embryo or Fetus (an unborn baby)
If you are pregnant, or become pregnant during participation in this research, the study drug might involve risks to an embryo or fetus, which are currently unknown. It is important that you contact the researcher immediately if you believe you might be pregnant.

Participation in Double-Blinded Studies
Participation in a double-blind study means that you may not be able to participate in other, similar trials since unblinding would generally only occur for emergent, life-threatening situations. We might

not be able to tell you if you received the study drug or placebo in a situation where you would like to qualify for another research study. Because you may not know the study group to which you were assigned, in the future should you wish to participate in a different study that requires knowing what drug you received in this study, you may not be eligible to participate in the different study. Unblinding will only occur when it is deemed medically necessary, and will only take place after consultation with the PI.

Follow-up Visit for Discontinuing Participants
While you are free to discontinue your participation at any time, we encourage you to complete a Final Study Visit. During this visit, we will conduct tests to collect safety data, and discuss any information that may be important to share with your treating physician.

Incidental Findings and Duplicate Tests
It is possible that the research procedures could uncover information related to your health that you did not know about before and that is unrelated to the Study. Some of these findings may be too preliminary to share. We will carefully consider the research findings and determine if they should be shared with you. Research findings would only be shared with you if such sharing is approved by the CSMC IRB and is permitted by applicable law. In some cases, additional clinical testing may be required. The cost of any additional testing and any related treatment will be your responsibility.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

If you agree to take part in this research study, there may or may not be direct medical benefit to you. If you are randomized to receive pravastatin, the possible benefit of taking part in the research study is that the study drug may delay or prevent HCC recurrence. However, no benefit is guaranteed. If you are randomized to receive placebo, you should not expect to benefit from taking part in this research study. In either case, it's possible that your condition may remain unchanged or even get worse.

We hope the information learned from this research study will benefit other individuals with HCC and cirrhosis in the future by helping us to learn whether pravastatin may delay or prevent HCC recurrence.

5. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:

- The study is stopped or suspended;
- Funding for the study is reduced, stopped or withdrawn;
- If treating physician judges that discontinuation in the study is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures;
- You demonstrate recurrence of HCC (unless continued treatment with study drug is deemed appropriate at the discretion of the investigator);
- You experience toxicity that makes continuation of the drug unsafe;
- You become pregnant;
- You develop a second malignancy (except for basal cell carcinoma or squamous cell carcinoma of the skin) that requires treatment, which would interfere with this study;

You may choose (or you may be required) to withdraw from certain parts of the study, but invited to continue with other parts. For example, you might stop taking a study drug, but continue with follow-up visits or allow us to continue to collect data from your medical records. Separate written consent will be requested if your continued participation will involve procedures not described in this consent form.

6. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive.

If you decide not to take part in this study, you have other choices. For example:

- you may choose to be treated following the usual clinical approach
- you may choose to take part in a different study, if one is available
- you could decide not to be treated.

The researcher will discuss these options and their risks and benefits with you.

7. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record. 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 identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, CSMC coordinating center Staff for safety and quality monitoring, and authorized representatives of the sponsor.

UCLA, NWU, UCSF, and EU participant data and specimens will be sent to CSMC in a coded manner. CSMC personnel will not have access to the key code; only the PIs and study staff from UCLA, NWU, UCSF, and EU will have access to the key code for participants at their institutions.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

As part of this research, it is necessary to restrict your right to access copies of health information created during your participation in your research while the research study is in progress. This restriction is necessary to maintain the blinding, in other words, it is important to the study outcomes that you not know into which treatment group you were assigned. Your right to access this information will be restored upon completion of the entire study if requested.

8. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

Contact your researcher at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your researcher of your situation at the phone number listed on page 1 of this consent form.

Who pays for my research related illness or injury?
Cedars-Sinai has no plans to pay for costs associated with the treatment of research-related injury or illness. We will make every effort to seek reimbursement from your health plan. However, you will be responsible for any deductibles and co-payments required under your health plan and for any claims ultimately denied by your health plan. Financial assistance may be available under Cedars-Sinai's Charity Care Policy and Procedure. If you feel that you have had a research-related injury and need financial assistance, please contact the IRB Office at 310-423-3783.

9. FINANCIAL CONSIDERATIONS

Costs of Participation
Please review the attached Appendix A flowchart for a listing of items, drugs and services that will be billed to you and/or your insurance and those that will be covered by the study sponsor.

Only items, drugs and services that are reasonable and necessary for your medical care throughout the study will be billed to your insurance. You remain responsible for all deductibles, co-pays, and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. You should check with your health benefit plan if you have questions or concerns about your insurance coverage.

Compensation for Participating
You will be paid for each study visit. Visits 1, 2, 3 and 5 will have a $75 compensation each. Screening, Visits 4 and 6 will have a $25 compensation. The total amount you will receive if you complete the whole study is $375. Payment will be issued after each visit date. If you do not complete the entire research study, you will only be paid for those visits and procedures you do complete. You may be required to complete a W-9 Form in order to receive payment. Although any amount of payment may be reportable (check with a tax professional if you have questions about your obligations), if total payment is $600 or more in a calendar year, a 1099 Form will be filed with the IRS in accordance with federal tax law.

If you are a Cedars-Sinai employee, you should provide your employee identification number to the research team so that your payment can be appropriately processed through Payroll. For your own protection and to comply with tax laws, your payment for participation will be reported to the IRS together with other compensation you receive from Cedars-Sinai.

Compensation will be managed by a private company contracted to issue a specially designed debit card onto which your compensation for research participation will be loaded. When a visit is completed, funds will be approved and loaded onto your card. The funds will generally be available within 5 business days, however, should you identify any concerns with an expected deposit, please contact the study team. You will be issued one card for the duration of your participation. If your card is lost or stolen, you will need to request a replacement.

To be able to issue you a debit card, we will need to share your name, address, social security number, and date of birth with the private company contracted to issue and manage the debit card. All information is stored in a secure fashion and is deleted from the debit card system once the study has been completed and the funds on the card have been exhausted. The private company will not share your information with any other third parties.

For patients who complete the Screening visit but are found to be ineligible for the study, the $25 compensation may be in the form of a check or other form of payment issued by Cedars-Sinai.

Financial Interest in the Research
The Principal Investigator and institution have no potential financial conflict of interest with respect to this study.

10. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact one of the investigators listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP) Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

11. CONSENT PROVISIONS

If you sign this form below, it means that:

(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights (other than the postponement of your access to certain health information as described in this informed consent form);
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and

(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights", if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and a signed copy of the Experimental Subject's Bill of Rights.

SIGNATURE BY THE PARTICIPANT:

_____	_____	_____
Name of Participant (Print)	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR:

I have personally explained the research to the participant in non-technical terms, answered all questions, and attest that he/she freely consents to participate. The participant has been provided with the Experimental Subject's Bill of Rights.

_____	_____
Signature of the Investigator Who Obtained Consent	Date of Signature

SIGNATURE BY THE INTERPRETER/WITNESS

(Signature of an interpreter is only required when a non-English speaking subject is consented with the assistance of an interpreter and an IRB-approved 'short form.' The witness may be any person who is conversant in both English and the language of the Non-English speaking subject, such as the interpreter (the certified hospital interpreter), study staff, a family member, or other person. The witness signs the consent forms to confirm that the oral interpretation occurred.)

Signature of Interpreter/Witness	Date of Signature

CEDARS-SINAI MEDICAL CENTER

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Distribution instruction for researchers:

The signed (i) Consent form, (ii) Authorization for Use and Disclosure of Identifiable Health Information and (iii) "Experimental Subject's Bill of Rights" (the latter required if the research study involves medical interventions)* should be distributed to:

1) Medical Chart
2) Research Participant
3) Pharmacy (if a drug study)
4) Principal Investigator's research records (original).

APPENDIX A: FLOWCHART OF PROCEDURES – Medicare Coverage Analysis (MCA) Review

FLOWCHART OF PROCEDURES – Medicare Coverage Analysis (MCA) Review

Procedures	**Screening Visit**	**Study Visit 1** (0-30 days from screening)	**Study Visit 2** (1 month after starting study drug)	**Study Visit 3** (3 months after starting study drug)	**Study Visit 4** (6 months after starting study drug)	**Study Visit 5** (9 months after starting study drug)	**Study Visit 6** (12 months after starting study drug)	**Follow-Up** (Day 30, 60, and 90 following study completion)
Standard of Care Procedures: Items and services that are part of regular care and would be done even if you did not take part in this research study. These will be billed to you and/or your insurance company.								
Physical Assessment (Including vital sings, height, and weight)	X				X		X	
Review medical history & medications				X	X	X	X	
Blood chemistry[1]	X				X		X	
Serum: α-fetoprotein (AFP)	X				X		X	
Imaging for HCC surveillance (Magnetic resonance imaging [MRI] with contrast, computed tomography [CT] scan, or ultrasound)	X			X	X	X	X	
Research Related Procedures: Items and services done for research purposes only. These will NOT be billed to your insurance company.								
Review eligibility criteria	X							
Review medical history & medications		X	X					
Obtain informed consent	X							
Imaging review (any SOC imaging)	X		X	X	X	X	X	
Registration & randomization to pravastatin or placebo	X							
Health assessment (Vital signs, weight, and ECOG)		X	X	X		X		
Blood chemistry		X	X					
Laboratory Blood Test: Lipid Panel		X	X				X	

Laboratory Blood Test: Hemoglobin A1c (glycated hemoglobin)		X			X		X	
Laboratory Blood Test: Prothrombin Time	X						X	
Laboratory Blood Test: Creatine Kinase[2]		X						
Urine Pregnancy Test for women able to become pregnant	X							
Liver stiffness (Magnetic resonance elastography or FibroScan)		X					X	
Liver fat fraction (Magnetic resonance elastography or Fibroscan)		X					X	
Conduct interviewer-administered questionnaire		X			X		X	
Dispense study drug and diary with instructions		X	X	X	X	X		
Research blood specimen		X			X		X	
Collect and complete compliance assessment of study drug diary and medication			X	X	X	X	X	
Assess Baseline symptoms		X						
Assess symptoms and adverse events			X	X	X	X	X	X
Telephone contact	X	Once a Month ⟶						X
If patient undergoes liver transplant before the end of this study end, liver tissue specimen and research blood will be collected at time of transplant.			When it becomes available ⟶					

[1] Any SOC labs that need to be repeated for research purposes will be billed to research.

[2] If the participant reports unexplained muscle pain or weakness, CPK will be tested again to check for elevation and will be billed to research.

APPENDIX B: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks

The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.

Study Procedure	Related Risks
Blood draw: A needle is placed in the vein in your arm to draw blood	Blood drawing may cause some pain and has a small risk of bleeding, bruising, or infection at the puncture site. There is also a small risk of fainting.
Abdominal magnetic resonance elastography (MRE): An MRE is a test that uses low-frequency vibrations that pass through your liver to make pictures of organs and structures inside the body. The MRE is incorporated into your MRI scan which you will be having as standard of care. At the end of the MRI session a small pad is placed on the surface of your body. The procedure is painless. You will hear a knocking sound as images are being taken and feel vibration around the liver area only during elastography series, the MRI technologist will notify you when the MRE series will begin. You will be able to communicate with the MRI technologist all the time and you will have a panic button to use if you want to stop the procedure at any time. The MRE will last about 5 minutes.	You may feel slightly anxious inside the scanner due to a fear of small enclosed spaces (claustrophobia). Also, at times, you may hear a knocking sound as images are being taken during the MRE session. You may be given headphones and may request ear plugs if you feel the noise is too loud. At any time, you may ask the technician to stop the exam if you are unable to complete the exam.
Liver elastography (FibroScan): A FibroScan is a test that uses mechanical pulse at the surface of the skin used as a non-invasive measurement of the liver. You will be asked to lie on your back with your right arm raised behind your head. The probe will be placed over a small amount of water based gel with slight pressure over your rib area. The Fibroscan takes about 10 minutes.	You may feel slight pressure of the probe that might make you uncomfortable.
Tissue Specimen Collection: A specimen collection is the removal of a sample of body tissue for examination under a microscope, by the doctor or scientist, to determine the state of health or disease in the tissue.	There are no risks associated with these procedures. The specimen collection will be from the native liver after it has been removed during the transplantation procedure (prior to discarding it).
Physical Exam: Includes height, weight, vital signs (heart rate and blood pressure)	There are no physical risks associated with these procedures.
Concomitant Medications: You will be asked about your previous and current medications	There are no physical risks associated with these procedures.

that you take.	
Medical History Review: You will be asked about your medical and surgical history with attention to your cirrhosis, HCC and your physical activity.	There are no physical risks associated with this procedure.
Pregnancy Test: If you are a woman who is able to become pregnant, urine samples will also be used to do a pregnancy test	If your test is positive, you will be told and at that point you should discuss options available with your primary physician.
Questionnaires: You will be asked to complete a questionnaire. We will ask you questions to evaluate things such as acculturation, quality of life; medical and medications history; alcohol and tobacco smoking. We think it should take about 45 minutes to complete the questionnaire. Questionnaires will ask you to respond to questions about your current alcohol consumption, eating habits, and birth and early life.	If you feel uncomfortable or embarrassed answering any question, you may skip it. The questionnaire will be labeled with a unique study number that will link your identity so that only the research team can recognize you.
Demographic Information: You will be asked about your age, gender, race, ethnicity	There are no physical risks associated with these procedures.

APPENDIX C:

Food and Medications to Avoid During Your Participation in the Study

Do not consume grapefruit products (grapefruit, grapefruit juice, grapefruit seed extract, or dietary supplements containing grapefruit) while you are participating in the study. Medications including, but not limited to, the following medications listed may interact with your study medication. Please do not use any of the following medications while you are participating in the study. Tell your study doctor immediately if you use any of these medications, or if any of these medications or any new medications, herbal medications, or supplements are prescribed for you during the study.

Generic name	Brand name(s)
azithromyocin	Zithromax, Zmax,
clarithromycin	Biaxin, Prevpac
colchicine	Colcrys
cyclosporine	Gengraf, Neoral, Sandimmune
erythromycin	EES, Erythrocin, Ery-Tab, E-Mycin
fibrates	Lipofen, Lopid, TriCor, Lofibra, Trilipix, Fenoglide, Antara, Fibricor, Triglide,
gemfibrozil	Lopid
niacin	Advicor, Niaspan, Niacor, Simcor, Slo-Niacin