UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

A phase IIa, randomized, double-blind, placebo-controlled study of the safety and efficacy of fenofibrate as a treatment for Huntington's disease

You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed below will be available to answer your questions.

RESEARCH TEAM
Lead Researcher
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Department of Neurology
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Dr. Hermanowicz's Pager: 714 506-9687

STUDY LOCATION(S):
Gottschalk Medical Plaza and Institute for Clinical and Translational Sciences (ICTS)

STUDY SPONSOR(S): Institute for Clinical and Translational Sciences (ICTS) and HD CARE

WHY IS THIS RESEARCH STUDY BEING DONE?
The purpose of this research study is to study the safety and efficacy of fenofibrate, an FDA-approved drug for high cholesterol and/or elevated triglyerides (fats), as a treatment for Huntington's disease (HD).

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 25 participants will take part in the research at UCI.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?
Please note this may not be a complete list of eligibility criteria. We have included a few examples of study criteria to help you better understand how your eligibility in the study will be determined; your study team will go through the study eligibility criteria with you to verify if you qualify for participation in this study.

Inclusion Requirements
You can participate in this study if you are:

- An adult of either sex, ages 25-85 inclusive,
- Have proficiency with written and spoken English and corrected vision or hearing to complete the cognitive testing,
- Are able to give informed consent,
- Have good overall health status with no known problems anticipated over the course of the trial,
- Have a diagnosis of HD supported by positive gene test within the past 6 months

Exclusion Requirements
You cannot participate in this study if you:

- Other major neurological disease [e.g., multiple sclerosis, parkinson's disease, cortical stroke, etc]
- Clinically significant hepatic or renal disease,
- Current or recent (< 1 month) use of dopamine blocking agents such as tetrabenazine, anticonvulsants, neuroleptics, HAART, antiemetics, and antipsychotics for any reason,
- Current use of Warfarin (Coumadin).
- Enrollment in another investigational drug study within the prior three months.
- Are pregnant.

HOW LONG WILL THE STUDY GO ON?
You will take fenofibrate once a day for six (6) months. You will have monthly follow-up visits, where you will have a fasting blood draw, a brief clinical examination and completion of an adverse events questionnaire. In addition, at the baseline, three and six month visits you will complete behavioral questionnaires. These monthly visits will take approximately 30 minutes to one (1) hour.

WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?
Before you can participate in the main part of the study...
You will need to have "screening" exams, tests or procedures. The screening process helps the researchers decide if you meet the study requirements listed below. The screening procedure includes a fasting blood sample for clinical blood work allowing assessment of renal and hepatic function. Any other significant abnormality in the blood work that in the judgment of the Study doctor would affect participation in the clinical trial would also be considered. All potential participants who meet the eligibility criteria after this screening will be considered eligible for the clinical trial.

Screening Visit. After consent, potential participants will be scheduled for the first study visit where they will provide or undergo the following tests:

- Medical history
- Family histry
- Current medication
- Blood sample will be taken to assess renal and hepatic function
- Vital signs
- General Physical Exam
- Neurological Exam

All potential participants will arrive to this morning visit fasting and having withheld all medications from the previous evening.

During the main part of the study…
If the screening exams, tests and/or procedures show that you can continue to be in the study, and you choose to take part, then you will have the following procedures and tests done. The main study tests and procedures include:

Baseline Visit. The baseline visit will be completed within one to two weeks of the Screening Visit and prior to the administration of any study medication. The study procedures include:

- A fasting blood sample for baseline leukocyte (white blood cells) PGC-1α protein and transcript levels (test of a specific protein and its message believed important to energy metabolism).
- Motor tests
- Cognitive tests
- Psychiatric tests
- Functional tests
- Review of study procedures
- Six (6) month supply of study medication will be distributed

Study Drug. Study subjects will be randomized 3:1 to receive either a six-month supply of study medication or placebo (an inactive pill that is made to look identical to the study medication) from the Study Coordinator at the baseline visit. All study medications (active drug and placebo) will be prepared in identical appearing capsules. The approved dosing of fenofibrate is in 48mg, 96mg, and 145mg capsules with a maximum dose of 145mg per day. Participants assigned to the active drug group will take a single 145mg capsule of fenofibrate daily during the study and participants assigned to the placebo group will take a single, identical appearing inert capsule daily during the study. We will utilize the maximum tolerated dose for each subject beginning at 145mg per day and reduce the dose if significant side effects are encountered.

Monthly Visits. The 6 monthly visits may take up to 2-3 hours and will involve a:

- Fasting blood draw
- Brief clinical examination
- Completion of an adverse events questionnaire
- A pill count will be done to monitor study drug compliance.

Monthly visits are expected to last 30 minutes to one hour. The 3- and 6-month visits will include administration of motor, cognitive, psychiatric and functional measures.

Following each fasting blood draw, participants will receive a small snack and beverage (for example, a small juice and energy bar). The clinical examination will be performed following your snack and beverage.

Table 1. Schedule of Visits

	Screening Visit	Baseline Visit	1-month visit	2-month visit	3-month visit	4-month visit	5-month visit	6-month visit
Consenting	X							
Review Inclusion/Exclusion Criteria	X	X						
Demographics and family and medical history	X							
Vital signs	X	X	X	X	X	X	X	X
Renal and hepatic blood tests	X	X	X	X	X	X	X	X
Concomitant medication review	X	X	X	X	X	X	X	X
PGC1-α levels	X	X	X	X	X	X	X	X
Fenofibrate levels		X	X	X	X	X	X	X
Motor, Cognitive, Psychiatric, Functional measures	X	X			X			X

Clinical neurological and physical examination	X	X			X			X
Study drug reconciliation and dispensing		X	X	X	X	X	X	X
Adverse events questionnaire			X	X	X	X	X	X

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. The researchers may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking fenofibrate. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to the research team about any side effects you experience while taking part in the study.

Risks and side effects related to fenofibrate may include:

Common risks (frequency is 1% to 10%)

- **Abdominal pain**
- **Back pain**
- **Asthenia (weakness)**
- **Flu syndrome**
- **Diarrhea**
- **Nausea**
- **Respiratory Disorder**
- **Rhinitis (nasal allergy)**

Less common risks (frequency is 0.1% to 1%)

- **Headache**
- **Abnormal liver function tests**
- **Constipation**
- **Hypertension (high blood pressure)**
- **Alterations in kidney function**

Rare (frequency is 0.01% to 0.1%)

- **Accidental injury**
- **Allergic reaction**
- **Chest pain**
- **Cyst**
- **Fever**
- **Hernia (an organ or fatty tissue that squeezes through a weak spot in a surrounding muscle or connective tissue)**
- **Infection**
- **Pain**
- **Angina pectoris (chest pain, pressure or squeezing in the chest)**
- **Arrhythmia (an unusal rate or rhythm of the heart)**
- **Atrial fibrillation (irregular and often rapid heart rate)**

- **Cardiovascular disorder**
- **Coronary artery disorder**
- **Abnormal electrocardiogram (unusual test of the electrical activity of the heart)**
- **Extrasystoles (a premature contraction of the heart)**
- **Hypotension (low blood pressure)**
- **Migraine**
- **Myocardial infarct (heart attack)**
- **Palpitation (perceived abnormal heart rate)**
- **Peripheral vascular disorder**
- **Phlebitis (inflammation of a vein)**
- **Tachycardia (rapid heart rate)**
- **Varicose vein**
- **Vascular disorder (vein disorder)**
- **Vasodilatation (dilation of the blood vessels)**
- **Venous thromboembolic events (deep vein thrombosis, pulmonary embolus) (a serious blood clot)**

- **Chronic indigestion**
- **Dark urine**
- **Muscle cramps, pain, stiffness, swelling, toxicity or weakness**
- **Trouble breathing**
- **Unusual bleeding or bruising**
- **Unusual tiredness**
- **Yellow eyes or skin**

Randomization: You will be assigned to a study group by chance (like a coin flip) rather than by a medical decision made by the researchers. The treatment you receive may prove to be less effective or to have more side effects than the other study group(s), or than standard treatments available for your condition.

Placebo: During this study there is a 25% chance that you will receive a placebo. This could lengthen the amount of time before you receive a treatment that may be effective. During this time, you may experience worsening of your condition, including increased HD symptoms. The researchers will carefully monitor your condition. You may of course withdraw from the study at any time.

Blood draw: Removing blood by a needle may cause temporary pain, bruising, bleeding, swelling, dizziness, and on rare instances fainting or infection.

Psychological discomforts: Some of the procedures may cause embarrassment or anxiety, or the questions the researchers ask you may be upsetting or make you uncomfortable. If you do not wish to answer a question, you can skip it and go to the next question. If you do not wish to participate you can stop.

Unknown risks: There may be risks related to the research that we don't know about yet. However, you will be informed of any additional risks to which you may be exposed, and any changes that are made to the study, as a result of any newly-identified risks.

Reproductive Risks: You should not get pregnant while in this study. The drug used in this study could harm an unborn baby. Check with the researchers about what types of birth control, or pregnancy prevention, to use while in this study. Contraception should be started 30 days prior to the baseline visit.

You should also not breastfeed a baby while in this study, as the drug used in this study could harm a newborn baby.

If you are a male, you should not father a baby while on this study.

If you or your partner does become pregnant during the study, you should contact the researchers immediately.

ARE THERE BENEFITS TO PARTICIPATING IN THIS STUDY?

Participant Benefits

Taking part in this study may or may not make your health better. While researchers hope fenofibrate will be more effective, than the standard (usual) treatment, there is no proof of this yet.

If you are in the group that receives fenofibrate and it proves to treat your condition more effectively, with fewer side effects than standard therapy than the placebo, you may benefit from participating in the study, but this cannot be guaranteed.

Benefits to Others or Society

This study will help researchers learn more about fenofibrate, and it is hoped that this information will help in the treatment of future patients with Huntington's disease.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

If you decide not to participate, or if you withdraw from this study before it is completed, your other choices may include:

- Getting no treatment
- Getting standard treatment for your condition without being in a study.
- Getting a different experimental treatment/taking part in another study.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

Compensation

You will not be compensated for your participation in this research study. You will receive a light snack and beverage following your fasting blood draw. Parking for study visits will be provided.

Reimbursement

You will not be reimbursed for any out of pocket expenses, such as transportation fees.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There is no cost to you or your insurer/third party payer for participation in this study.

You and /or your health plan/insurance will be billed for the costs of any standard medical care you receive to diagnose and/or treat any medical condition(s) outside of this study. You will be responsible for any deductibles or co-payments that would normally be associated with these standard medical costs.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number listed at the top of this form.

If you are injured as a result of being in this study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California, or billed to you or your insurer just

like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call UCI Human Research Protections (949) 824-6068 or (949) 824-2125 or by e-mail at IRB@research.uci.edu

WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?
You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, the study sponsor decides to stop the study or your safety and welfare are at risk.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you withdraw or are removed from the study, the researcher may ask you to return for a final close-out visit or evaluation and return unused study medication.

If you elect to withdraw or are withdrawn from this research study, you may choose to terminate the continued use or disclosure of your protected health information (PHI) for research purposes. The request to end the use or disclosure of your PHI should be made in writing.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?
Subject Identifiable Data

Some identifiable information collected about you will be kept with the research data. Your medical record number and date of birth will be maintained to obtain your laboratory results from the electronic UC Irvine Health medical record system.

Data Storage
Research data will be maintained in paper format in a secure location at UCI. Only authorized individuals will have access to it.

Research data will be stored electronically on a secure network in an encrypted file with password protection.

Data Retention
The researchers intend to keep the research data for approximately six (6) years.

WHO WILL HAVE ACCESS TO MY STUDY DATA?
The research team, authorized UCI personnel, the study sponsor, and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

Any information derived from this research project that personally identifies you will not be released or disclosed by these entities without your separate written consent, except as specifically required by law. Research records provided to authorized, non-UCI entities will not contain identifiable information about

you. Publications and/or presentations resulting from this study will not include identifiable information about you.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy

ClinicalTrials.gov is a Web site that provides information about clinical trials. 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.

ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?

Use of Specimens
Any specimens (e.g., tissue, blood, urine) obtained for routine labs will be discarded or destroyed once they have been used for the purposes described in this consent.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

A 24-hour number is also listed on the top of this form to report any health concerns or unanticipated problems you may experience after normal hours or on weekends.

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact UCI's Office of Research by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@research.uci.edu or at 141 Innovation Drive, Suite 250, Irvine, CA 92697.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?
You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep. **Participation in this study is voluntary.** You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.

I agree to participate in the study.

Subject Signature	**Date**
Printed Name of Subject	
Legally Authorized Representative/Guardian Signature	***Date***
Printed Name of Legally Authorized Representative/Guardian	***Relationship to Subject***
Legally Authorized Representative/Guardian Signature	***Date***
Printed Name of Legally Authorized Representative/Guardian	***Relationship to Subject***
Signature of Person Obtaining Informed Consent *(Individual must be listed on Page 1 of this consent)*	**Date**
Printed Name of Person Obtaining Informed Consent	

A witness signature is required on this consent form only if: (Researchers: check which one applies)

☐ Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐ The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

For the witness:
I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____

Witness Signature **Date**

(If no witness signature is required, this witness signature section of the consent form may be left blank).

_____

Printed Name of Witness

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@research.uci.edu; or by writing us at 141 Innovation Drive, Suite 250, Irvine, CA 92697.