Cover Page

Title: Exploration of Gemfibrozil as a Treatment for AUD

Clinical Trial Number: NCT03539432

Consent Document Date: 6/29/2018

MIND RESEARCH NETWORK
CONSENT TO PARTICIPATE IN RESEARCH

Exploration of gemfibrozil as a treatment for AUD
6/29/18

Purpose and General Information

You are being asked to participate in a research study that is being done by Eric Claus, Ph.D., who is the Principal Investigator, and his co-investigator Claire Wilcox, M.D. This research is being done to evaluate whether the medication gemfibrozil is an effective treatment for alcohol use disorder. This medication is approved by the Federal Drug Administration (FDA) for the treatment of hyperlipidemia (which is a condition where individuals have a high concentration of fats or lipids in their blood). Some early research in animal studies has shown this medication may help reduce drinking, but use for the treatment of alcohol use disorders is considered experimental, and this medication is not FDA approved for the treatment of alcohol use disorders. Therefore, the goal of this study is to see if it helps people with alcohol use disorder decrease or stop their alcohol use. This study also will try to identify, using questionnaires, cognitive testing, and brain imaging [functional magnetic resonance imaging (MRI)] which people are most likely to respond to this medication, and how this medication works.

You are being asked to participate because you are interested in reducing or stopping your drinking. Approximately 20 people will take part in this study. The study will take place at the Mind Research Network. This pilot study is funded through support provided by the Mind Research Network.

This form will explain the study to you, including the possible risks as well as the possible benefits of participating. This is so you can make an informed choice about whether or not to participate in this study. Please read this consent form carefully. Ask the investigators or study staff to explain any words or information that you do not clearly understand.

What will happen if I participate?

If you agree to be in this study, you will be asked to read and sign this consent form. After you sign the consent form, the following things will happen:

You will first undergo a consenting process which involves reading through this form, and discussing any questions you may have with the research staff. You will then answer a series of questions about your drinking and psychiatric history, and also complete other questions (e.g. handedness, metal in the body) to determine if you qualify for the study. Females will also complete a urine pregnancy test. In addition, a medical screening will take place in which a medical doctor will conduct a medical history and physical examination, and trained research staff will conduct a blood draw.

If you are eligible for the study, you will then be randomized to one of two groups: an active treatment group or a placebo group (a placebo is a pill that looks like the active medication, but has no active medication in it). Randomization means you will be assigned to a treatment based on chance, like a flip of a coin. Neither you nor any member of the research team chooses your assigned group or will know what group you are assigned to, however, in an emergency (e.g., if you are hospitalized or in an accident and knowing the drug would be important for your treatment), the study doctor can get this information. You will have an equal chance of being in either group.

Participation in the study will take a total of approximately 15.5 face-to-face hours and an additional half hour over the phone, which will occur over about 7 weeks. The study schedule is as follows:

- Two screening visits: consent visit (2 hours) and physical exam visit (2 hours).
- A baseline visit (visit 3, 4.5 hours): to complete questionnaires, MRI scanning, short talk therapy session and medication dispensed (active or placebo).
- Talk therapy (visit 4): One 45 minute session, one week after starting the medication
- Follow up visit (visit 5, 3.5 hours): Two weeks after taking medication - questionnaires, MRI scanning, blood draw, urine drug test and pregnancy test (females only), brief talk therapy session, and additional two weeks of medication. Trained research staff will conduct the blood draw.
- Follow up visit (visit 6, 2.5 hours): Four weeks after taking medication - questionnaires, blood draw, and the final talk therapy session. Trained research staff will conduct the blood draw.
- Phone call: Six weeks after taking medication, we will contact you to do a brief, 30 minute interview.

You will be provided the medication/placebo for a total of four weeks.

We have organized the different components of the study below into three categories (Screening, Treatment and Assessment), which we will describe in more detail below.

I. Study Eligibility Screening

As part of screening to see if you qualify for the study, we will ask you about your alcohol and drug use in the previous 90 days, conduct a structured interview asking you about psychiatric symptoms and substance use history, ask questions about which hand you use to do various tasks, and ask you questions to determine whether it is safe for you to go in the MRI. If you are eligible, you may be asked to return for a physical exam and so that we can obtain your medical history. In addition, about 2 teaspoons of blood will be drawn with a needle from a vein in your arm and will be checked for kidney function, electrolytes, liver function, and blood cell counts; this initial blood draw will occur at the first or second visit. You will be informed of the results of the laboratory tests. If you request, we will also call your doctor about any abnormal blood work results after you sign a release of information. The study physician will review some of your questionnaire results, medical history, and drug and alcohol use history with you, and is always available to answer any questions you may have.

At Visits 1, 3, and 5, you will have a breath alcohol test and a urine screen to test for illegal drugs and pregnancy (in females of child bearing potential). At all visits, you will be asked about alcohol use, drug use, and alcohol craving.

II. Treatment

Pending your lab results, if you are enrolled in the study, the study physician will explain the study medication in detail to you, including dosing and possible side effects, and will discuss ways for you to remember to take your medication. At Visit 3, you will start either the treatment medication or the placebo medication. You will have your medication dispensed to you at Visit 3 and Visit 5.

At the visits we will review side effects and any adverse events with you, check your blood pressure and heart rate, and depending on necessity, may have some other physical exam tests done. In addition to the medication, you will also be able to complete 4 sessions of counseling (i.e. talk therapy), which is a widely utilized treatment known to help people cut down or stop drinking. At the end of the study, we will also offer you a resource list for other potential treatment facilities in the community.

Participation in this research will include audio taping of your session with the counselor. The audio tape will be used for training and quality control purposes and may be coded in the future

to answer research questions. The tapes will only be identified by your subject number. Individuals who will have access to these tapes will be the principal investigator and the study counselors.

III. Assessments

At some visits, you will be asked to fill out questionnaires which will ask about mood and anxiety symptoms and alcohol craving, and you will be asked to perform some cognitive tests on the computer and using paper and pencil. You will also complete brain MRI scans during two of the study visits. During the MRI scan you will be asked to perform a few tasks, including looking at alcohol-related images and/or unpleasant pictures. You may refuse to answer any questions or perform any test that you do not wish to answer or do.

Finally, you will be asked more questions about alcohol and drug use over the phone at the end of the study.

If you arrive at a study visit intoxicated, the visit will be cancelled, and you will not receive your medication refill until you are under the legal limit. Furthermore, you will not be allowed to drive home until you are under the legal limit for alcohol. In cases of intoxication, the assessment will be rescheduled to occur as quickly as possible. You may be discontinued from the study at any time if you miss study visits or scheduled medication doses.

MRI: During the study you will undergo a brain study called an MRI; you will do this procedure twice (Visit 3 and Visit 5). To undergo the MRI sessions, we will ask that you abstain from alcohol and all illicit drugs for at least 24 hours beforehand, that you not be in alcohol withdrawal, and that you remember to take your medication dose that morning. If the MRI results are unclear, you may be asked to have an additional MRI done. For this study, you will lie down on a table and will then be placed into a long donut-shaped magnet. During the study you will hear loud rapping and knocking noises coming from the magnet. You may feel warm during this procedure. In order to obtain good pictures, it is important that you do not move during the procedure. Although you should not talk during the MRI procedure, you will be able to talk with the technician during breaks or in case of emergency by pressing a call button or similar device. During the scan, you may be shown pictures and words and will be asked to make decisions about the information presented in them. This takes about 1 hour to complete.

The MRI scan is being done to answer research questions, not to examine your brain for medical reasons. This MRI scan is not a substitute for a clinical scan (the type a doctor would order). The research scan might not show problems that may be picked up by a clinical MRI scan. However, all research MRI scans will be read by a neuroradiologist (a doctor with experience reading MRI scans) unless you have been scanned at MRN in the previous six months. When your scan is read, you will receive an e-mail letting you know you can download your MRI report from the Participant Portal Homepage. If we find an abnormality that requires follow-up, we may also mail a copy of the report to you, or contact you and your doctor (with your permission) by phone to help answer questions. Our Medical Director or the research team is always available to answer any questions you may have about your scan.

Urine sample: You will be asked to provide a urine sample to test for the presence of several drugs, including cocaine, heroin, methamphetamine, and marijuana. You will be able to collect the sample in a bathroom without anyone watching you. The results of these tests will not be shared with police, security, parole officers, or anyone outside the study team, even if you test positive for a drug. If you are

a female, we will also test for pregnancy using your urine sample. Urine drug/pregnancy tests will take place at Visits 1, 3 and 5.

What are the possible risks or discomforts of being in this study?

Medication: There are certain risks associated with taking the study medication. These include:
Not serious, common (>1%)

- stomach upset
- stomach/abdominal pain
- nausea
- vomiting
- diarrhea
- fatigue
- rash
- dizziness
-

Serious, uncommon or rare (<1%)

- anemia (decreases in red blood cell counts), leukopenia (decreases in white blood cell counts), thrombocytopenia (decreases in platelet counts)
- appendicitis
- persistent nausea or vomiting
- yellowing eyes or skin
- dark urine
- gallstones
- liver problems
- rhabdomyelisis (muscle inflammation, breakdown)
- atrial fibrillation (irregular heart rhythm)

We will check for side effects at every visit and the study physician may choose to discontinue the medication if you are showing signs of serious side effects.

MRI: Radio and magnetic waves associated with MRI scans are not associated with any known adverse effects. MRI is non-invasive and considered minimal risk by the FDA. However, the scanner is a large magnet, so it could move objects with iron in them in the room during the scan. This means that loose metal objects, like coin currency or key chains, are not allowed in the MRI room. If you have a piece of metal in your body such as a pacemaker, nerve stimulator, piercings or certain metal surgical implants, you will not be allowed into the MRI room and cannot have an MRI. While in the scanner, you may be bothered by feelings of claustrophobia (fear of small spaces). If you feel uncomfortable (nervous or upset stomach) in the MRI scanner for any reason, tell the research staff. The MRI also makes loud 'drum' beating noises during the study. Headphones will be provided for your safety and comfort. There is a speaker in the MRI scan room as well as a window that allows the operator to view you during data collection. This allows the assistants to hear and see you at all times to ensure that you are comfortable and to allow them to respond if you are uncomfortable. You can stop the scan at any time.

No long-term harmful effects from MRI are known. However, since the effect of MRI on early development of the fetus is unknown, participants who are pregnant should not go in the MRI. If you are a woman you will be asked to take a urine pregnancy test before being allowed to participate in the study.

You are the only person who will get the results; we will not report the results of the pregnancy test to anyone else. Rarely, large tattoos can heat up during an MRI scan and cause skin irritation like a sunburn, so the MRI technologist will want to see any tattoos you have prior to the scan.

Due to the very high sensitivity of MRI in detecting abnormalities, there is a risk of false-positive findings, identifying something on imaging studies that may or may not be important. This may result in anxiety and additional testing, possibly including a recommendation for clinical scans at your cost. The radiology report or other study data will not be put into your medical record unless you provide it to your physician. If the radiology report becomes part of your personal medical record, it may or may not have an effect on getting health insurance or life insurance in the future.

Participation in this study may produce emotional stress, inconvenience or an invasion of privacy. In addition, there may also be side effects or risks to study participation that are unexpected and not known at this time. Every effort will be made to protect the information you give us. However, there is a small risk of loss of confidentiality that may result in stigmatization. Procedures we will use to protect the information you give us are described below.

How will my information be kept confidential?

We will take measures to protect your privacy and the security of all your personal information. Your name and other identifying information will be maintained in locked files and/or restricted databases, available only to authorized members of the research team for the duration of the study. All of the information we collect about you will be coded with a unique research subject identifier (URSI) or other subject code and will be kept on password protected computers according to MRN information security policies. The record linking your name to your study ID number will be kept indefinitely (forever) at the MRN in a confidential manner so that you may continue to have access to your information. De-identified data (meaning data that cannot be traced back to you) from this study may also be presented at meetings, published in journals/books, used in classrooms for training/teaching purposes, and may be shared with other researchers, which includes scientists at other universities and institutions. However, your name and other identifying information will not be used in any published reports about this study.

To help us protect your information, this research study has applied for a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, the research team cannot be forced to provide your name or any identifiable research data or specimens to people who are not connected with this study, including Federal, state or local authorities, even under a subpoena. The protection offered by the certificate does not stop us from reporting information about suspected or known sexual, physical, or other abuse of a child or older person, or that you plan to harm yourself or someone else. If any member of the research team is given such information, we will make a report to the appropriate authorities. Information from your participation in this study may be reviewed by MRN, federal and state regulatory agencies, and by the University of New Mexico Institutional Review Board (IRB) which provides regulatory and ethical oversight of human research.

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 are the benefits to being in this study?

You may or may not have benefit from the study. Knowledge gained through this study may aid the development of more effective treatments for individuals with alcohol dependence and other addictive

disorders. There are also potential direct benefits to participants in this study. Everyone (whether assigned to the active treatment with gemfibrozil or placebo group) will receive treatment throughout the study with an evidence-based psychosocial intervention provided by the study team, and will also be offered a referral list upon completion of the study. If the medication being tested works, then individuals assigned to the intervention group may also benefit from the treatment. Also, being in a research study may provide benefit, as may taking a placebo pill; individuals who undergo a series of assessments in a research study oftentimes reduce their drinking even if they are not on active treatment.

In the course of this research, brain scans will be performed on you. These scans will be used solely for the purpose of gathering scientific information for this study. During the study, you will not be provided a medical diagnosis or treatment for any brain condition, or other health problem.
Finally, your participation may help find out if gemfibrozil is an effective treatment for alcohol use disorder, and, if it is helpful, the mechanism by which it is working.

What other choices do I have if I don't participate?
Taking part in this study is voluntary so you can choose not to participate. We will still provide a list of treatment providers if you decide not to participate.

New information that may impact your decision to participate
You will be informed of any significant new findings that become available during the course of the study, such as changes in the risks or benefits resulting from participating in the research or new alternatives to participation that might change your mind about participating. If any new information related to the medication used in the study becomes available, study staff will inform you of the new information and you will be able to discuss this information with the PI or study physician to determine whether it changes your decision to participate.

Are there any costs to me for participating?
You will not be charged for any of the experimental study procedures, including the MRI scan. If incidental findings from the study result in the need for further evaluation/treatment, then you or your insurance company will be responsible for any clinical evaluation/treatment that may be needed.

Will I be paid for taking part in this study?
In return for your time and the inconvenience of participating in this study you will be paid up to $250 total for participation via gift cards or cash. The payments will be allocated as follows: consent and screen visit $20, history, physical and screen visit $20, baseline assessment (visit 3) $60, counseling session (visit 4) $10, second assessment/counseling (visit 5) $80, third assessment/counseling (visit 6) $50, final phone assessment $10.

If MRN and/or the investigators develop intellectual property and/or commercialize products or services, directly or indirectly, based on the results of the research done with your data, there are no plans to provide you with any financial compensation.

Compensation for participation in research is considered taxable income and should be reported on your income tax return. If you earn $600 or more participating in MRN research studies, you will be sent a W-9 form to collect your tax information which will be reported to the Internal Revenue Service (IRS) as required by law. The information provided to the IRS will not disclose your participation in a research study; instead the income will be listed as "nonemployee compensation."

THE MIND RESEARCH NETWORK

Can I stop being in the study once I begin?
Yes. You can withdraw from this study at any time without affecting your access to care, education, or other services to which you are entitled. If you decide you would like to stop the study medication during the study, please let your study doctor know as soon as possible and we will help you discontinue it.

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, if you do not follow study procedures, or if it is in your best interest or the study's best interest to stop your participation. MRN may stop the study at any time.

What will happen if I am injured or become sick because I took part in this study?
If you are injured or become sick as a result of this study, the University of New Mexico Health Sciences Center (UNMHSC) will provide you with emergency treatment, at your cost. No commitment is made by the MRN or UNMHSC to provide free medical care or money for injuries to participants in this study.

It is important for you to tell the Principal Investigator immediately if you have been injured or become sick because of taking part in this study.

Refusal to Sign
If you choose not to sign this consent form, you will not be allowed to take part in the research study.

What if I have questions or complaints about this study?
If you have any questions, concerns or complaints at any time about the research study, Eric Claus, Ph.D., or his associates will be glad to answer them at 505-272-5028. If you would like to speak with someone other than the research team to obtain information or offer input, or if you have questions regarding your rights as a research participant, please contact the IRB. The IRB is a group of people from UNM and the community who provide independent oversight of safety and ethical issues related to research involving people: UNM Office of the IRB, (505) 277-2644, irbmaincampus@unm.edu. Website: http://irb.unm.edu/

Consent
You are making a decision whether to participate in this study. Your signature below indicates that you read the information provided (or the information was read to you). By signing this consent form, you are not waiving any of your legal rights as a research participant.

OPTIONAL:
We would also like to request your permission to store all of the data that was collected in this study in The Mind Research Network Data Sharing Repository for other, future research. The stored data will include information such as your age and gender, as well as assessment and imaging data that were collected about you during the course of this study. It is possible that this information may remain linked to your name. It will be handled with the same care and confidentially as it is for the current study. Research done with information from the data repository could lead to improved diagnostic and treatment interventions for illnesses and brain disorders. If published, results will be presented in summary form only and will not include your name or other identifying information. If MRN develops intellectual property and/or commercialize products or services, directly or indirectly, based on the results of the research done with your data, there are no plans to provide you with any financial compensation.

You have my permission to store my data in the MRN Data Sharing Repository for future research. Please initial next to your choice below.
YES _____ Initials
NO _____ Initials

We would like to request your permission to contact you for participation in future studies at the Mind Research Network. If you agree, your contact information may be shared with other scientists at MRN.

You have my permission to contact me about participation in future research studies. Please initial next to your choice below.
YES _____ Initials
NO _____ Initials

I have had an opportunity to ask questions and all questions have been answered to my satisfaction. By signing this consent form, I agree to participate in this study. A copy of this consent form will be provided to me.

_____ _____/_____
Name of Adult Participant (print) Signature of Adult Participant Date

I have explained the research to the participant and answered all of his/her questions. I believe that he/she understands the information in this consent form and freely agrees to participate.

_____ _____/ _____
Name of Research Team Member Signature of Research Team Member/Date