Title:

Lemborexant Augmentation of Naltrexone for Alcohol Craving and Sleep: A Randomized, Double-Blind, Placebo- Controlled Study

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CONSENT FORM
Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals
Main Consent

H-52091- LEMBOREXANT AUGMENTATION OF NALTREXONE FOR ALCOHOL CRAVING AND SLEEP: A RANDOMIZED, DOUBLE-BLIND, PLACEBO- CONTROLLED STUDY

Concise and Focused Presentation

You have been invited to participate in a voluntary study while receiving treatment at The Menninger Clinic. The purpose of this study to evaluate the effects of naltrexone plus lemborexant augmentation compared to naltrexone plus placebo on alcohol cravings and sleep in people with alcohol use disorder and insomnia. We will use a virtual reality technology to expose you to alcohol-related scenarios to determine the effectiveness of the medications in reducing alcohol cravings. This will mimic alcohol exposures outside of the hospital. We will also measure how well you are sleeping using a sleep watch and questionnaires. The procedure (described below) is in line with standard-of-care at Menninger. There is a risk that you will have side effects with the study medications. You may benefit from this study by having reduced alcohol cravings and sleep improvement. However, you may not receive any benefits. You do not have to participate in this study and can continue to receive your normal care.

Background

You are being asked to participate in this voluntary research study because you are receiving inpatient care at the hospital. Please read this information and feel free to ask any questions before you agree to take part in the study.

Many people with alcohol use disorder struggle with alcohol cravings and insomnia even while they are in the hospital, which can interfere with your engagement in treatment and lead to longer recovery times. Naltrexone is an FDA-approved and extensively studied medication to reduce alcohol cravings. Lemborexant is FDA-approved for insomnia and has had studies establishing effectiveness and safety. In this study, we want to know if lemborexant combined with naltrexone can further reduce alcohol cravings and improve sleep. Relief of these symptoms can improve mental health symptoms such as depression and suicidal thoughts.

Purpose

This study aims to evaluate the effects of lemborexant combined with naltrexone on alcohol cravings and insomnia and how this can have impact on your mental health. Ultimately, the goal of this project is to save lives by examining and addressing alcohol cravings and sleep problems in those who are struggling with alcohol use disorder and insomnia. Analysis of the data we collect from you will allow us to evaluate current treatment options, advance future treatments, and broaden the base of knowledge of treatment of mental health disorders.

Procedures

The research will be conducted at the following location(s):
Baylor College of Medicine and The Menninger Clinic.
This study will examine the effectiveness of a medication combination for alcohol cravings and sleep while you are at The Menninger Clinic. In this study, you will be randomly assigned to either naltrexone plus Lemborexant or naltrexone plus placebo group. At the end of each week, we will ask you to go through a virtual reality environment with scenarios involving alcohol use. After you go through the virtual reality scenario, we will ask you to fill out a questionnaire about your alcohol cravings (Alcohol Urge Questionnaire). We will also ask you to fill out a questionnaire about your alcohol cravings during the week (Penn Alcohol Craving Scale). To determine how well you are sleeping, you will be asked to wear a sleep watch 24/7 with exception of the shower. All of these will be done while you receive other treatment at The Menninger Clinic. Other clinical outcomes questionnaires such as the severity of your depression and anxiety are collected as part of standard of care at The Menninger Clinic. The data collected from these questionnaires and the sleep watch will measure your progress in treatment.

All your data from the questionnaires and sleep watch will be stored securely, where only approved research staff will have access. All your data will be kept completely de-identified and anonymous; any identifying information will never be disclosed in future research work.

Clinically Relevant Research Results
The results generated from this research study are not expected to have any clinical relevance to you.

Sharing and Future Research Studies with Identifiable Private Information
Your identifiable private information collected as part of this research , even if the identifiers are removed, will not be used or distributed for future research studies.

Research related health information
Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine and The Menninger Clinic to use or disclose (release) your health information that identifies you for the research study described in this document.
The health information that we may use or disclose (release) for this research includes:

• Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
• Specific information concerning alcohol abuse
• Specific information concerning drug abuse
• Demographic information (name, D.O.B., age, gender, race, etc.)

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, and The Menninger Clinic.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine and The Menninger Clinic are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and The Menninger Clinic to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research involves treatment. You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment. To maintain the integrity of this research study,

you generally will not have access to your personal health information related to this research until the study is complete. However, your health information that is necessary to your care will be provided to you or your physician. At the conclusion of the research and at your request, you generally will have access to your health information that Baylor College of Medicine and The Menninger Clinic maintain in a designated record set, which means a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Baylor College of Medicine and The Menninger Clinic to make decisions about individuals. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by representatives of the specific institution where you are being enrolled into this research study which are: Baylor College of Medicine and The Menninger Clinic.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, regulatory agencies such as the U.S. Department of Health and Human Services, Baylor College of Medicine, and The Menninger Clinic may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: Thanh Truong at 12301 S. Main Street Houston, TX 77035.

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts
Research involving greater than minimal risk because you will be taking medications. However, the study presents the prospect of helping you sleep better and have reduced alcohol cravings.

Lemborexant: the most common side effects associated with lemborexant are drowsiness, headache, abnormal dreams, fatigue. Uncommon side effects include sleep paralysis, hallucinations before you fall asleep and upon waking, and sleep behaviors such as sleep walking, sleep eating, and making phone calls during sleep. Lemborexant in combination with central nervous system depressants (i.e., alcohol, sedative/hypnotics) may cause more drowsiness than either drug alone. Any addition of depressants during the treatment such as sedative/hypnotics will be discouraged. However, it is possible that, in spite of warnings against use of sedative/hypnotics while in the study, you may elect to use them. Any use of sedative/hypnotics will be documented and monitored for medication interactions. You will receive checks by nursing staff every 15 minutes as part of the standard hospital care even while asleep. You will also have access to nursing 24/7 and will receive support if there are any concerning behaviors or other side effects.

Naltrexone: the most common side effects associated with naltrexone are nausea, abdominal pain, diarrhea, vomiting, headache, anxiety, dizziness and insomnia. Uncommon side effects include skin rash,

drowsiness, and depression. Naltrexone rarely causes temporary, mildly increased serum transaminases, though it is not associated with significantly cases of liver injury. As would any medication, there is a potential for an allergic reaction with naltrexone or lemborexant. If at any point you experience uncomfortable side effects and wish to stop the medication(s), the medication(s) will be discontinued and nursing staff are informed immediately.

There may be some discomfort in wearing the ActiGraph wrist-watch. This may be alleviated by asking nursing staff or research staff to provide band-aids, soft gauze, or other such materials. You will be wearing this watch throughout your stay at Menninger, other than in and around water (i.e., showers, pool).

There may be discomfort when going through the virtual-reality scenario involving alcohol. You may experience emotional discomfort and alcohol cravings after the experience. However, these feelings may reflect how you will respond to exposure to alcohol outside of the hospital and while in the hospital, you will be provided support from nursing staff and the treatment programming. If at any point you become distressed or wish to stop, the protocol is discontinued and nursing staff are informed immediately.

Discomfort surrounding the disclosure of any of your personal information is alleviated by assurances of confidentiality and security of any personal information. The risk for loss of confidentiality is minimal, as data storage is secure, and only approved research staff will have access to data. Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits
The primary benefit of participation in this study for subjects is the potential for reduction of alcohol cravings and insomnia in those receiving the study medication. Additionally, there is a potential for reduction in symptoms of depression and improvement in your and your clinician's impression of quality of life. If the treatment is found to be effective, other individuals with similar problems may benefit from the findings of this study. However, you may receive no benefit from participating.

Alternatives
You may choose to not participate in this study.

Subject Costs and Payments
You will not be asked to pay any costs related to this research.

Subject's Rights
Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these

benefits, services, or rights.

The investigator, Thanh Truong, and/or someone she appoints in her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: Thanh Truong at 713-275-5251 during the day and after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research , if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date