Consent to Participate in a Research Study
REPOSE Study: Efficacy of suvorexant to improve postoperative sleep and reduce delirium severity in older surgical patients: A double-blinded, randomized, placebo-controlled trial

CONCISE SUMMARY

The purpose of this study is to evaluate Suvorexant to improve postoperative sleep and decrease the rate of and severity of delirium, a syndrome of confusion that occurs after surgery.

After your surgery when it is time to go to sleep at night, you will receive either Suvorexant 20mg or a placebo (a placebo is an inactive substance given in the same form as the active drug, Suvorexant). You will receive this again for up to three nights while in the hospital following surgery.

During the time you are enrolled in the study, you will wear a headband for the first 3 nights after surgery to measure your sleep, complete questionnaires assessing your sleep, perform delirium and alertness assessments, have your pupil size measured, and have blood samples collected at various times.

Prior to your surgery, you might also have the opportunity to wear a wristband device that measures your sleep at home.

Your participation in the study will last 4 weeks, the last visit being a telephone call.

The risks of the study are described in this document. Some of the risks include drowsiness, headaches, unusual dreams, cough, and diarrhea.

If you are interested in this study, please continue reading below.

You are being asked to take part in this research study because you are having surgery and are expected to stay in the hospital overnight. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

[Principal Investigator Name] will conduct the study and it is funded by [Funder or Sponsor Name]. [Funder or Sponsor Name] is funding this study and will pay [Location Study is Being Performed] to perform this research, and these funds may reimburse part of [Principal Investigator Name]'s salary.

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WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, [Principal Investigator Name] will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to determine whether Suvorexant administered after surgery improves sleep and reduces the severity of delirium in older surgery patients. After surgery, older patients sometimes experience delirium, a disturbance of mental abilities resulting in confused thinking and reduced awareness. Suvorexant is approved by the FDA for the treatment of insomnia, a disorder that involves difficulty falling or staying asleep. Suvorexant may help improve sleep in hospitalized older patients after surgery and reduce delirium severity, but this is unknown. Therefore, this study is investigating whether Suvorexant improves sleep and decreases delirium severity in older surgery patients.

Sleep deprivation is associated with problems with the immune system, which helps fight infection, heart disease, earlier onset dementia, and increased death rates. Thus, there is increasing focus on improving sleep in vulnerable patient populations such as older surgical patients, because they are at increased risk for postoperative complications and susceptible to sleeping problems before and after surgery.

Since delirium is associated with higher hospitalization costs and postoperative complication rate, there is a critical need to find an FDA-approved medicine to decrease delirium. There is also a need for safe and effective sleep medicines for older hospitalized patients. Commonly used hypnotic sleep aids such as benzodiazepines (Xanax, Ativan, Klonopin) and non-benzodiazepines (Lunesta, Sonata, Ambien) are avoided in hospitalized patients because they increase delirium, but this leaves older hospitalized patients with few, if any, options for safe sleep aids.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately [Number of Anticipated Enrollment] people will take part in this study at [Location Study is Being Performed].

WHAT IS INVOLVED IN THE STUDY?
If you agree to be in this study, you will be asked to sign and date this consent form. If you do not sign consent form, you will continue to receive care, but not as part of this study.

Outlined below is what will be asked of you while participating in the research study.

You will be randomly assigned (like the flip of a coin) to receive either Suvorexant or placebo**.** You have a 50/50 chance of receiving study drug.

Before Surgery

- Confirm eligibility to participate in the study.

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- Record medical history and current medications.
- Assessments and questionnaires that evaluate sleep quality, insomnia severity, memory, and delirium.
- Psychomotor vigilance test that uses a computer to measure your reaction time for attention and alertness
- Pupillometry, to measure small spontaneous fluctuations in pupil size
- Optional: Prior to surgery and while at home, we may provide you with a wrist activity monitor which is a device worn on your wrist that determines your sleep patterns by measuring your rest/activity cycles. If you decide to participate in the wrist activity monitor, we would ask you wear it a minimum of 3 days to maximum of 6 weeks.

Day of Surgery

➢ Prior to Surgery
- Confirm your eligibility to participate in the study
- If not completed at time of consent - sleep quality, insomnia severity, memory and delirium assessments and questionnaires; psychomotor vigilance test and pupillometry that measures spontaneous fluctuations in your pupil size.
- Blood sampling to examine inflammation by measuring proteins called interleukin 6 - about ½ tablespoon (10 milliliters)
- Randomization- like a flip of a coin to determine if you will be assigned to take Suvorexant or a placebo. (a placebo is an inactive substance given in the same form as the active drug, Suvorexant)
- Medication review

➢ After Surgery
- Delirium assessment at night after surgery
- Confirm eligibility to receive study drug.
- Administration of Suvorexant or placebo
- Measure your sleep with the EEG headband device (which looks at brain waves). The headband placement will be placed no earlier than 4:30pm and removal of the headband will be prior to 10am the next morning.
- Pupillometry, to measure small spontaneous fluctuations in pupil size

Note: If your surgery happens to go later than 8pm, due to the operative period crossing into the study drug and sleep period, the activities listed above would not be performed on the night of your surgery. The administration of Suvorexant or placebo and sleep measurement with the EEG headband device would instead first be administered the next night on post-op day 1 and would occur each night until post-op day 3 (or until discharge if that occurs sooner.)

Post-op Day 1 & 2 (or until discharge if occurs sooner)
- Delirium assessment in the morning and again in the afternoon

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- Sleep quality assessment
- Confirm eligibility to receive study drug.
- Administration of Suvorexant or placebo
- Measure your sleep with EEG headband device (which looks at brain waves). The headband will be placed no earlier than 4:30pm and removal of the headband will be prior to 10am the next morning.
- Psychomotor vigilance test
- Pupillometry
- Blood sampling- about ½ tablespoon each day (10 milliliters each day)

Post-op Days 3, 4 & 5 (or until discharge if occurs sooner)

- Delirium assessment in the morning and again at night
- Sleep quality assessment

Note: If on your day of surgery, the surgery happens to go past 8pm, the following activities could be performed on post-op day 3:

- Confirm eligibility to receive study drug.
- Administration of Suvorexant or placebo
- Measure your sleep with the EEG headband device (which looks at brain waves). The headband will be placed no earlier than 4:30pm and removal of the headband will be prior to 10am the next morning.

4-week post-op

- Phone call to see if you are having any health problems.

HOW LONG WILL I BE IN THIS STUDY?
You will be in this study for 4 weeks, with the last visit being a phone call. You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

WHAT ARE THE RISKS OF THE STUDY?
As a result of your participation in this study, you may be at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose. Suvorexant may cause some, all or none of the side effects listed below.

Most common side effects of Suvorexant:

- Headache
- Diarrhea
- Dry Mouth

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- Cough
- Abnormal Dreams
- Dizziness
- Drowsiness

Less common side effects of Suvorexant include:

- Sleep paralysis
- Sleep walking
- Itchiness
- Nausea
- Vomiting
- Palpitations
- Daytime sleepiness and impairment
- Worsening of depression and suicidal ideation

Risks of Drawing Blood:
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

Risks of Wearing the EEG headband device:
Risks associated with wearing the EEG headband device include slight discomfort caused by the forehead sensors placed against the skin. Approximately 0.1% of patients may have a red spot on their forehead as a result of wearing the sensor for an extended period of time.

Drug and Food Interactions
For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
There are currently no known benefits of Suvorexant administration in older adults after surgery. Since Suvorexant has been shown to decrease time to sleep onset and improve sleep maintenance in outpatients with insomnia, Suvorexant has the potential to improve postoperative sleep, which could improve patient satisfaction and postoperative cognition as well as prevent the development of delirium after surgery.

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WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests and procedures may be reported to the study sponsor. In addition, your records may be reviewed to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, the Institutional Review Board, research staff and non-research staff (for billing and health care operations). If any of these groups review your research record, they may also need to review your entire medical record.

The study results will be retained in your research record for [Insert length of time] At that time, either the research information not already in your medical record may be destroyed or information identifying you will be removed from such study results. Any research information in your medical record will be kept indefinitely.

Some information collected in research studies is maintained in your medical record. However, for this study that information will be inaccessible until the end of the study, unless your physician(s) decides that it is necessary for your care.

This information may be further disclosed by the funder of this study. If disclosed by the funder, the information is no longer covered by federal privacy regulations. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of [Location study is being performed], we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

WHAT ARE THE COSTS TO YOU?
You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all

services are covered by insurance. Some procedures or scans may require pre-authorization by your insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the study with [Principal Investigator's Name]**.** At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

The study sponsor has agreed to pay for services and procedures that are done solely for research purposes. Please talk with the principal investigator/ study team about the specific services and procedures that the sponsor will pay for, and the ones for which you or your insurance will be responsible.

We will monitor your patient care charges to make sure that costs are directed appropriately. If you have any questions or concerns about appropriate billing, contact your study team coordinator so that he/she can help find a resolution.

[Study Sponsor or funder] will provide the study drug free of charge to you. Your study doctor may request that you stop the study drug before the normal end period, if he/she thinks that continuing the study medication could result in harm to you.

WHAT ABOUT COMPENSATION?
You will be compensated up to a maximum of $75 for your expenses related to your participation.

- If you wear the EEG headband for at least 1 night after surgery, you will be compensated $50 at time of discharge from the hospital for your participation in the study.
- You will be compensated an additional $25 if you choose to wear a wrist band monitor (which measures your sleep patterns) at home for 3 nights before surgery.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at [Location] in the event that you are injured as a result of your participation in this research study. However, there is no commitment by [Name of location], your physicians, or the study supporter or funder to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, [Insert PI Contact Information Here].

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WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?
You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care. If you do decide to withdraw, we ask that you contact [Insert PI Contact Information Here].

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent.

The use of your data and samples may result in commercial profit. You will not be compensated for the use of your data and samples other than what is described in this consent form.

A description of this clinical trial will be available on https://clinicaltrials.gov/ as required by U.S. Law The clinical trial number for this study is NCT05733286. This Web site 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.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact [Insert PI contact information here].

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact [Insert information here].

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OPTIONAL ACTIVITY TO CONSENT TO

Optional wrist activity monitor (Please initial one)

_____ Yes- I wish to participate in the home wrist activity monitor measurement.

_____No- I do not wish to participate in the home wrist activity monitor measurement.

STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____ _____ _____
Signature of Subject Date Time

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____ _____ _____
Signature of Legal Representative Date Time

_____
Relationship to Subject