COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
200 FR. 4 (2016-2)

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

Study Title: *Efficacy and Safety of Sugammadex (2mg/kg) to shorten time-to-extubation among postoperative ICU patients following AVR, CABG, or AVR/CABG surgery- a prospective randomized placebo-controlled trial.*

Principal Investigator: *Amit Bardia, MD*

Funding Source: *Merck Pharmaceuticals*

Invitation to Participate and Description of Project

You are invited to take part in a research study designed to look at whether the medication Sugammadex decreases the time it takes to remove the breathing tube (extubation) after cardiac surgery. You have been asked to take part because you are undergoing a Coronary Artery Bypass Graft (CABG), or an aortic valve replacement (AVR), or an AVR/CABG combination procedure and will have a breathing tube after your surgery.

We expect to enroll approximately 110 subjects in this randomized, double blind, placebo-controlled trial. We anticipate completing enrollment in approximately 1 year.

There are medications routinely used during cardiac surgery that cause relaxation and/or paralysis of your muscles. They make putting the breathing tube in easier (intubation) and minimize muscle movements during surgery. The medications that cause this relaxation or paralysis are called Neuromuscular Blockers (NMB). These medications are sometimes associated with prolonged intubation and there are some risks associated with that.

We are studying the effect of the FDA approved medication Sugammadex used to reverse the neuromuscular relaxation caused by anesthesia in adults undergoing heart surgery on the length of time it takes patients to be ready to have the breathing tube removed (extubation) in the ICU. Sugammadex is known to rapidly reverse medications that provide neuromuscular blockade and it is not associated with the cardiovascular side effects commonly seen with other NMB reversal agents.

To decide if you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, that a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures and possible benefits and possible alternative treatments. Once you

understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

Your anesthesia plan will be left to the discretion of the anesthesiologist caring for your during your cardiac surgery. After your surgery is complete you will be transferred to the CTICU with a breathing tube (intubated) and on a propofol and/or dexmedetomidine (Precedex) infusion. These medications are sedatives and are routinely used in patients having cardiac surgery.

When you arrive to the Cardio-Thoracic Intensive Care Unit (CTICU), your surgeon and CTICU intensivist will do an initial assessment and decide if you are able to proceed on a fast-track removal of your breathing tube.

A member of the study team will also review the post-operative inclusion/exclusion criteria. If it is decided that you are eligible to continue to the fast-track pathway, your sedatives will be discontinued 30 minutes after the ICU admission and you will be randomized to receive sugammadex versus placebo. Randomization means your treatment assignment is random or by chance, like the flip of a coin with heads and tails being equal chances. A placebo is a substance that looks like the real drug but doesn't contain any active ingredients. Routinely no medication is given at this time and the NMB medication is allowed to wear off. The study investigators will not know what treatment you receive. The study drug or placebo will be administered through an existing intravenous lines by the nurses caring for you in the CTICU under the direction of a study investigator. These nurses are specifically trained to administer the medication and are aware of its actions. The study drugs will be received from the investigational drug pharmacy in a blinded fashion. This means the study doctor will not know if you received active medication or placebo.

Ten minutes after the drug administration, if you can lift your head and your blood pressure is stable, the setting on the ventilator will be changed to allow you breath more on your own. If after 30 minutes you have been able to take deep breaths and maintain your oxygen level the breathing tube will be removed.

If after 30 minutes, you can't breathe well enough without assistance from the ventilator, every effort will be made to help correct that. If corrected, assisted breathing and removal of the breathing tube will be reattempted. If you are still having difficulty you may need to go back to having the ventilator breath for you.

If extubation is successful, you will continue to receive standard post-operative care in CTICU. Your participation in the study will be complete once you are extubated.

You will be told of any new findings that may affect your decision to participate in the 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.

Risks and Inconveniences

Anesthetic management will be left to the discretion of the attending anesthesiology provider and that where sedation is desired and appropriate, patients will be transferred to the CTICU intubated and sedated. All of these medications that are routinely used as standard of care in patients undergoing coronary artery bypass graft surgery at Yale New Haven Hospital will be utilized.

Sugammadex is an FDA approved medication that reverses the effects of certain medications that are given during surgical procedures to relax your muscles. It is often used at the end of surgery, to help restore muscle function that has been blocked during surgery by the other medicines. In this study Sugammadex will be used in the CTICU with an aim to significantly decrease the time to extubation. The use of Sugammadex is associated with the following adverse reactions: Pain, nausea, vomiting and hypotension in more than 10% of the patients who have received this medication.

Headache, fever, high blood pressure, cough, chills, dizziness, trouble sleeping, EKG changes, high or low heart rate, itching, dry mouth and low calcium have been reported in 1-10% of patients receiving sugammadex.

Bleeding was originally thought to be a potential side effect of sugammadex, but studies have since shown that the risk is very low.

Sugammadex may cause some medications to be less effective, including hormonal contraceptives. If you are on any kind of contraceptive medication you should discuss this with a physician involved with this study. You cannot be included in the study if you are pregnant.

There is the possible risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

There may be additional risks related to this study that are not yet known

Benefits

Potential benefits associated with participation include: early extubation; you may spend less time in a critical care setting; and you may have a decreased risk of pneumonia.

The study does have placebo, so you may not experience any benefit.

Economic Considerations

You will not be paid for your participation. The medication, sugammadex will be provided by Merck Pharmaceutical. You will receive the standard of care after your surgery that you would ordinarily receive after surgery. You or your insurance company will be responsible for that care.

Treatment Alternatives/Alternatives

The only alternative is to not participate. If you do not participate you will be extubated per the

standard of care at the discretion of the CTICU attending physician.

Confidentiality and Privacy

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. We will have access to this information, but will not keep any identified or personal health information (PHI) as part of your participation in this study. You will be assigned a study number. OnCore, Yale's secure research data base will be utilized for study data. When data is downloaded for analysis you will only be identified by your study number.

Data will be collected on an encrypted and password protected laptop computer as an added measure to safeguard your confidentiality.

Authorized representatives of the Yale Human Research Protection Program and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects) may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential.

The database that contains your assessment data will stay on the computer until the study is completed. Once the study is completed your participant number will be removed and the data will be kept in this anonymous form indefinitely.

If the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

The information about your health that will be collected in this study includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this Study.
- The entire research record and any medical records historical and current held by YNHH created from: Admission to study completion.
- Records about your study visits

Information about you and your health which might identify you may be used by or given to:

- *The U.S. Department of Health and Human Services (DHHS) agencies*Representatives from Yale University, the Yale Human Research Protection Program and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
    - Those providers who are participants in the Electronic Medical Record (EMR) system.
    - Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
    - The Principal Investigator Dr. Amit Bardia
    - Health care providers who provide services to you in connection with this study

including Co-Investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study
- Merck Pharmaceuticals the funding agency and provider of Sugammadex

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale-New Haven Hospital are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g. health insurance company, disability provider.)

This authorization to use and disclose your health information collected during your participation in this study will never expire.

In Case of Injury

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured because of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

You do not give up any of your legal rights by signing this form.

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. Prior to extubation you will be groggy but alert. If you change your mind and don't want to proceed please let the study doctor know.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. After you have consented, had your surgery and are admitted to the CTICU, the Investigators on the study will reassess your eligibility to participate in the fast-track pathway. If you don't meet the criteria they will not proceed with the study. You will be extubated at the discretion of the CTICU physician.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital or, at your request, refer you to a clinic or doctor who can offer this treatment.

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to Dr. Amit Bardia, 333 Cedar St., TMP 3, New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study.
When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given

to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Name of Subject:_____

Signature:_____

Date:_____

_____ _____
Signature of Principal Investigator Date

or

_____ _____
Signature of Person Obtaining Consent Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203-432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator *Dr. Amit Bardia at 203-785-2802.* If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.