Title of Study: Reversal of Neuromuscular Blockade in Patients with Severe Renal Impairment; STU-2018-0411

CONSENT TO BE PART OF A RESEARCH STUDY
TO BE CONDUCTED AT

Parkland Health & Hospital System

Key Information about this Study

This study is being done to see if one drug that is used to reverse neuromuscular blockade (temporary paralysis of your muscle during surgery so that you don't move) is better than an older drug. Up until 2016, the drug used to reverse neuromuscular blockade in the USA was neostigmine. On December 15, 2015, the FDA approved a new medication for this same purpose called sugammadex, which became available at Parkland in 2016. The newer drug has a higher acquisition cost than the older drug but has been shown in numerous studies to be faster and better (i.e., more complete recovery) than the old drug.

This study is being done to see if paralysis with rocuronium and reversal with sugammadex is superior (better) than paralysis with cisatracurium and reversal with neostigmine. The latter is the current standard of care and what you would likely receive if you chose not to participate in the study. If you chose to participate in the study, there is a 50% chance you will get randomized (like picking straws) to the older drug and 50% chance you will get randomized to the newer drug.

The research team will follow you while you are in the operating room and for 30 days following surgery to make sure you don't get discharged from the hospital and have to come back or that you don't have any other unexpected events. You will have continuous pulse oximetry (a sticker on your finger) for 24 hours after surgery. If you are on dialysis, you will resume your normal dialysis schedule once you are out of surgery. This study is not intended to directly benefit the participants, although it is possible and we hypothesize that patients who get the newer drugs will recovery faster and have less complications, but this is not guaranteed, and we cannot assign which group you will be in. The additional risks beyond what you would already have with the anesthesia and surgery are that you might be allergic to one of the drugs we give you. Otherwise, the rest of your anesthetic care and surgery would be exactly the same as if you were not participating in the study.

Information About This Form

You may be eligible to take part in a research study. This form provides important information about the study.

Please take the time to review this information carefully. You should talk to the researchers about the study and ask them any questions that you may have. You may also want to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

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

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

Voluntary Participation

You do not have to participate if you don't want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Tiffany Moon MD., Department of Anesthesiology and Pain Management at UT Southwestern Medical Center and Parkland Health Hospital System.

Conflict of Interest
Merck, a for-profit company, is funding this study. The Principal investigator designed the study and drafted the study plan. Merck is providing money to UT Southwestern Medical Center, so that the researchers can conduct the study. The PI received grant funding and honoraria from Merck in 2018. Honoraria will not continue in 2019, but grant funding will.

Purpose – "Why is this study being done?"

Prior studies show that recovery from neuromuscular blockade (medicine that relaxes your muscles so the surgeon can do the surgery) with rocuronium is significantly faster with sugammadex (a new drug that just recently became available in the USA in 2015) versus cisatracurium and neostigmine (old drugs that are currently being used). Use of sugammadex has been shown to be safe in patients with a history of end stage renal disease. This study is being done to determine whether muscle paralysis with rocuronium can be more quickly and better reversed with sugammadex when compared to reversal of cisatracurium-induced neuromuscular blockade with neostigmine in patients with severe renal impairment.

- **Researche**r means the study doctor or research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals such as Parkland Heath Hospital System.
- **Standard medical care** is the regular care you would receive from your doctor if you choose not to participate in this research.
- **Neuromuscular blockade** is paralyzing skeletal muscles with muscle blockers such as rocuronium or cisatracurium during surgery.
- **Reversal agents** are medicines such as sugammadex and neostigmine that recover paralyzed skeletal muscle at the end of the surgery.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website 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.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because your kidneys are not working well, and you are scheduled to undergo surgery that requires us to paralyze your muscles.

How many people are expected to take part in this study?

This study will enroll a total of about 60 study participants.

Information about Study Procedures – "What will be done if you decide to be in the research?"

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. These procedures are described below as "standard care" and would be done even if you do not take part in this research study.

Screening Procedures
- The results of the physical examination done as part of your standard care will be used.
- If you are capable of becoming pregnant, a pregnancy test will also be done before you receive study treatment.
- Your eligibility will be determined by reviewing your medical record.
- Your heart rhythm (ECG) or radiological results will be also reviewed.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you.

Assignment to Study Groups
When it is determined that you are eligible for the study, you will be assigned by chance (like flipping a coin) to) to receive either rocuronium and sugammadex or cisatracurium and neostigmine+glycopyrrolate in the operating room

1) Cisatracurium / neostigmine + glycopyrrolate. Your muscles will be paralyzed with cisatracurium during surgery and then neostigmine + glycopyrrolate will be used to recover your muscles at the end of the surgery.
2) Rocuronium / sugammadex. Your muscles will be paralyzed with rocuronium during surgery and then sugammadex will be used to recover your muscles function at the end of the surgery.

Neither you nor the researchers will know which muscle blockers and reversal agents you receive during surgery. In the event of an emergency, there is a way for the researcher to find out which medication you received.

Study Procedures - as a participant, you will undergo the following procedures:
- You will be randomly assigned to one of the two study groups.
- In the operating room, your muscles will be paralyzed with muscle blockers cisatracurium or rocuronium. This is standard of care.
- You will be randomized to receive either neostigmine or sugammadex for reversal of neuromuscular paralysis. Sugammadex or neostigmine are approved by FDA to recover muscles paralysis. Neostigmine is commonly used reversal agent in the standard practice. Sugammadex is a new drug. Both reversal agents are standard of care.
- You will complete a questionnaire before the surgery and again after surgery. This questionnaire will be filled out 3 times: at 15 minutes, 40 minutes, and 80 minutes after surgery. (research only). It will take approximately 1-2 minutes.
- You will fill out a brief questionnaire on postoperative days 1 and day 2, either in your hospital room or over the phone from home. It will take approximately 3-5 minutes. (Research only).

You will be in this study approximately 30 days from the start of anesthesia until 30 days after surgery.

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.

Risks – "What are the risks of participation in the research?"

The investigators have designed this study to learn how well the new treatment(s) compare to commonly accepted treatment(s).

There is not much additional risk by participating in this study, above the standard risks associated with surgery and general anesthesia. There is a 0.3% chance that you may be allergic to sugammadex. The anesthetic management of subjects will not differ from the standard care.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately about any side effect that you have while taking part in the study.

The following section will describe the risks related to your participation in this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Risks from the specific research procedures (drug(s)

Side effects can range from mild to serious. Serious side effects are those that may require hospitalization, are life threatening or fatal (could cause death). The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

Risks of Rocuronium

The most common adverse reactions after administration of rocuronium are nausea, vomiting, light headedness, and minor changes in blood pressure.

	Frequent	Occasional	Rare
Serious		Residual neuromuscular blockade	Severe allergic reaction
Less Serious			
Minor	Nausea, Vomiting, Light Headedness, Minor changes in blood pressure	Injection site pain, Itching	

Risks of Cisatracurium

The most common adverse reactions after administration of cisatracurium are nausea, vomiting, light headedness, and minor changes in blood pressure.

	Frequent	Occasional	Rare

Serious		Residual neuromuscular blockade	Severe allergic reaction
Less Serious			
Minor	Nausea, Vomiting, Light Headedness, Minor Changes in blood pressure	Injection site pain, Itching/rash	

Risks of Neostigmine

The most common adverse reactions after administration of neostigmine are nausea, vomiting, and low heart rate, but another drug called glycopyrrolate is always given along with neostigmine to counteract the potential drop in heart rate.

	Frequent	Occasional	Rare
Serious			Severe allergic reaction
Less Serious	Low heart rate	Low blood pressure, low oxygen level	
Minor	Nausea, Vomiting, Dry mouth	Injection site pain, Itching	

Risks of Glycopyrrolate

The most common adverse reactions after administration of glycopyrrolate are dry mouth, nausea/vomiting, and headache.

	Frequent	Occasional	Rare
Serious			Severe rise in body temperature Abnormal heart rhythm
Less Serious		High heart rate, Trouble urinating, blurred vision, light sensitivity	High or low blood pressure
Minor	Nausea, Vomiting, Dry mouth	Itching, Dry skin, diarrhea, constipation	

Risks of Sugammadex:

The most common adverse reactions after administration of sugammadex are allergy, nausea/vomiting, pain, hypotension, and headache.

Sugammadex is mainly expelled from the body through the kidney (i.e., via urine). It is an FDA approved drug but not recommended if there is severe renal impairment, meaning that your kidneys don't work very well. The reason for this is because there have not been very many studies done on this patient population. Sugammadex may take longer to clear from your body since it comes out through urination, and patients with severe renal impairment (meaning your kidneys don't work very well) may not make much urine. *Think of sugammadex like a donut and rocuronium like a donut hole.* Since sugammadex wakes your muscles back up by attaching to rocuronium (the drug that puts your muscles to sleep) to form a sugammadex-rocuronium complex, people sometimes fear that sugammadex and rocuronium will become separated and there is a very theoretical concern that patients could become weak again. This has never been reported to happen. In the previous studies that have been done, it has been shown that sugammadex attaches to rocuronium very strongly, meaning that once the donut attaches to the donut hole, you cannot separate the two. One

study published in 2013 stated that for every 25 million sugammadex-rocuronium complexes formed, only 1 becomes separated, demonstrating that the risk is very low.

Hormonal birth control pills may be less effective when sugammadex is used as a reversal agent and increases the risk of the pregnancy for **7 days after surgery**.

- Female participants who are using hormone (birth control pills) have to use a barrier method (hormone-free birth control methods) such as condoms and spermicide for **7 days.**
- If you chose to participate, research team will give you a letter in your language with the information regarding birth control after surgery and phone number of the PI if they have any additional questions.

	Frequent	Occasional	Rare
Serious			Severe Allergic Reaction Low heart rate
Less Serious		High or low blood pressure	
Minor	Nausea, Vomiting, Pain, Headache	Itching, Dizziness	

Psychological Stress

There is minimal risk for psychological stress to the patient as a result of participating in this study. You may refuse to answer any of the questions, take a break, or stop your participation in this study at any time.

Loss of Confidentiality

Any time information is collected there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Other Risks

There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

For more information about risks and side effects, ask one of the researchers or study staff.

Reproductive Risks

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how the muscle relaxant and their reversal agents might affect a developing fetus. We will do a pregnancy test before your study enrolment to make sure you are not pregnant. If you participate in the study, you must use one of the barrier methods or back up method of birth control for a period of **7 days after the surgery**. If you do not wish to do so, you will not eligible for the study.

Are there Risks related to withdrawing from the study?

If you decide to withdraw from this study early, please discuss your decision with the principal investigator. The researcher may ask you to complete a study withdrawal form. There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

Are there risks if you also participate in other research studies?

Being in more than one research study at the same time, may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – "How could you or others benefit from your taking part in this study?"

You may not receive any personal benefits from being in this study. However, there may be potential for a direct benefit to you if you are assigned sugammadex group. Investigators intend to evaluate if sugammadex is superior to neostigmine for reversal of muscle function at the end of the surgery.

We hope the information learned from this study will benefit other people with similar conditions in the future.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

If you chose not to participate in the study, you will undergo general anesthesia with standard of care medications.

.

Costs – Will taking part in this study cost anything?

You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as the surgery, general anesthesia, and postoperative care. You will not be charged for any muscle blockers or reversal agents if you decide to participate in this study.

It is important to understand that some insurance companies do not cover some costs. If your insurance company does not cover these treatments or procedures, you will be required to pay for them. Ask the researchers if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

HIPAA Section:
Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include:

Your medical history and blood work, information that we get from your medical record, information contained in your underlying medical records related to your medical history and treatments prior to the study, information that is created or collected during your participation in the study including medical, surgical and treatment history, your physical status, weight, height, body mass index, blood pressure, heart rate, respiration, continuous heart rhythm, blood oxygen level, any adverse event during surgery, anesthetic agents, muscle blocker, and reversal of muscle function for general anesthesia, temperature, depth of the anesthesia, information you give us during your participation in the study such as demographic information like your age, questionnaires including your pain, emotion, and satisfaction. protected heath information including your name, date of birth, medical record number, and phone number.

We will get this information by asking you, your doctor, and looking at your chart at Parkland Hospital.

How will your PHI be shared?
Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- The following collaborators at other institutions that are involved with the study: Parkland Health & Hospital System
- The committee that checks the study data on an ongoing basis, to determine if the study should be stopped for any reason
- The members of the local research team.
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out.
- The Research offices at: The University of Texas Southwestern Medical Center, Parkland Health and Hospital System.

- The Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.
- Representatives of domestic and foreign governmental and regulatory agencies may be granted direct access to your health information for oversight, compliance activities, and determination of approval for new medicines, devices, or procedures.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information for review. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties, but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Tiffany Moon MD. Department of Anesthesiology and Pain Management at UT Southwestern Medical Center, 5323 harry Hines Blvd, Dallas, TX, 75390-9068. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

Because of the type of research, you can only access your PHI when the study is done. At that time, you have the right to see and copy the medical information we collect about you during the study, for as long as that information is kept by the study staff and other groups involved.

How long will your PHI be used?
By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends, and all required study monitoring is over.

Contact Information –
Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact: Tiffany Moon, MD at (469) 419-5790 during regular business hours and by pager at (214) 768-2038 after hours and on weekends and holidays.

To use the pager, you need to have a touch tone (push button) telephone. Dial the pager number as you would any phone number. When you hear 3 short high-pitched beeps, dial in the number where you want the doctor to call you back. Push the # button, hang up and wait for the doctor to return your call.

Primary Contact:
Tiffany Moon, MD. can be reached at (469) 419-5790 during regular business hours and by pager at (214)768-2038 after hours and on weekends and holidays.

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the HRPP by calling the office at (214) 648-3060.

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research, sign this section. You will be given a copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE FOLLOWING STATEMENTS ARE TRUE:

- You have read (or been read) the information provided above.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.
- You have freely decided to participate in this research, or you are voluntarily giving your consent for another person to participate in this study because you believe this person would want to take part if able to make the decision and you believe it is in this person's best interest.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.
- You authorize the collection, use and sharing of your protected health information (another person's protected health information) as described in this form.

Adult Signature Section

			AM PM
Printed Name of Participant	Signature of Participant	Date	Time
			AM PM
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date	Time