Official Title:
Pharmacokinetics, Pharmacodynamics, and Safety of a Single Dose Intravenous Methadone in Healthy Adult Volunteers (MTH02)

NCT#:
NCT05425420

Informed consent document date:
18Oct2023

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
ADULT
Pharmacokinetics, pharmacodynamics, and safety of a single dose intravenous methadone in healthy adult volunteers (Version 4.0 dated 18Oct2023)

IRB No: Pro00106216 **DEPRU No:** NL01 **Protocol No:** NL01-MTD

CONCISE SUMMARY

The purpose of this study is to provide information on how the body distributes, processes, and excretes the drug methadone. Methadone is approved by the U.S. Food and Drug Administration (FDA).

If enrolled, you will undergo screening procedures to see if you qualify. If you qualify and wish to continue, you will be asked to return to the Duke Early Phase Clinical Research Unit (DEPRU) for an overnight stay. In addition, there will be 3 follow-up visits, which will occur after discharge. Your participation in this study will last approximately 4 days, the screening visit will occur up to 30 days before your inpatient stay. You will have the following procedures performed at various times throughout the study: physical exam, vital signs, ECGs, pupil size measurement, pain sensitivity tests, and blood collections. Methadone will be administered intravenously [(IV) a small tube placed in your arm].

There are risks to this study that are described in this document. Common risks of methadone are: mild sedation, nausea, and vomiting. One of the uncommon risks is shortness of breath.

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

You are being asked to take part in this research study because you are a healthy individual 18 – 39 years of age who does not have known health conditions. 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 site 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 site staff if you are taking part in another research study.

"Site staff" means any person at the site investigator's location. The "study team" includes people involved with the study at the National Institute of Child Health and Human Development (NICHD), the IND Sponsor (the person in charge of the study overall) and Duke University.

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A contract from the National Institutes of Health of Child Health and Human Development (NICHD) will sponsor this study. These funds may reimburse part of Dr. Shruti Raja and her research team's salaries.

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, Dr. Shruti Raja 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 provide information on how the body distributes, processes, and excretes the drug methadone, to update the drug label. Methadone has been approved by the U.S. Food and Drug Administration (FDA) since 1947. However, medical technology has advanced greatly since then and we would like to further study how methadone is distributed, processed, and excreted from the body so that doctors can use this information to better treat their patients of different ages.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 30 people will take part in this study at Duke Early Phase Clinical Research Unit (DEPRU). It may be necessary to screen up to 30 people to ensure 20 people complete the study.

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. You will have the following tests and procedures to make sure that you are eligible:

Screening Visit (-30 to Day 0)
- Physical exam, including measuring your height and weight
- Female subjects of childbearing potential will have a pregnancy test (blood sample)
- Medical history, including substance abuse or addiction history
- Review of your current/recent medications
- The following vital signs will be collected: breathing rate, heart rate, and blood pressure, and measurement of your oxygen levels will be measured using a pulse oximeter on your finger.
- Screening labs to check for liver and kidney disease
- Introduction to study procedures, including the pupillometry goggles, pain testing, and self-assessment questionnaire
- Urine collection will be used to test for the following illegal and prescription drugs:
    - Methamphetamine (MET)
    - Morphine-a drug in the opiate class (MOR/OPI)
    - Marijuana (THC)
    - Amphetamine (AMP)

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  - Barbiturates (BAR)
  - Benzodiazepines (BZD)
  - Cocaine (COC)
  - Phencyclidine (PCP)
  - Methadone (MTD)
  - Ecstasy/MDMA (XTC)
- Breathalyzer test to check recent alcohol consumption
- Electrocardiogram (ECG) to measure the electrical activity of your heart which can tell us if there are any problems with heart rhythm. An ECG is performed by placing patches on your chest, which are connected by wires to a machine that records your heart's electrical activity

If you meet all the inclusion criteria and qualify for the study, you will be required to refrain from the following:

1. All alcohol for 24 hours before and during study days.
2. All caffeine-containing beverages on the day of study drug administration.
3. All food for 8 hours before study drug administration.
4. All liquids for 4 hours before study drug administration.
5. Non-study medications including over-the-counter (OTC) and herbal medications for 2 days prior to study drug administration without prior study doctor approval.

Study Days 0-1, (0-30 hours after-dose) Inpatient Visit
You will be admitted to the Duke clinic overnight, which will last approximately 30 hours. The study drug methadone will be administered by IV infusion. At the start of the inpatient stay, you will have two venous catheters placed. The venous catheters will be placed into your arm and/or hand. One of the IVs will be used to give you the study drug called Methadone. The second IV will be used to take blood samples for testing. If both IVs are in the same arm, the one below the study drug tube will be used for the PK blood samples. You will be free to move around and be given a standard meal 4 hours after completion of methadone hydrochloride administration. You will have free access to food and water while in the DEPRU. In addition, blood sampling, and drug effect assessments, and labs will be collected [kidney and liver function tests, and electrocardiogram (ECG) will be performed]. The following will occur at the inpatient visit:

- Review of your current/recent medications.
- Study participants may be tested for COVID-19, using a nose swab to test your nasal secretions for traces of COVID-19. COVID-19 testing will occur if you have new onset symptoms of COVID-19, or report COVID exposure within the last ten days.
- Urine collection to test for any drugs of abuse (illegal or prescription) and a breathalyzer (to see if you have been drinking alcohol recently).

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- The following vital signs will be collected: breathing rate, carbon dioxide concentration, which will be measured using a nasal cannula, like that used to give oxygen (plastic tube with two small prongs placed in your nose). In addition, heart rate, and blood pressure, and measurement of your oxygen levels will be measured using a pulse oximeter on your finger.
- Female subjects of childbearing potential will have a pregnancy test (urine sample).
- Prior to study drug administration and 24 hours after study drug administration an ECG will be used to test for any problems with your heart rhythm.
- To decrease or prevent nausea you will receive 4mg IV ondansetron. If nausea persists you may receive IV metoclopramide.
- Pharmacokinetic (PK) blood samples will be collected to measure the amount of the study drug, methadone, in your blood. This information helps researchers determine the appropriate dosage and frequency of methadone administration. Blood will be collected via IV catheter.
- Pupil size will be measured using a goggle-based, camera-like device.
- You will be assessed on how sleepy or alert you are using a score of 0-5, 0 being asleep and unresponsive and 5 being very alert.
- Self-assessment of methadone effect, will be conducted using the Visual Analog Scale (VAS). You will be asked to use a scale from 0 to 100 to rate different factors such as, sleepiness, energy level, clumsiness, confusion, anxiety, and nausea.
- We will measure how sensitive you are to pain by using a thermal pain stimulator. This device applies heat to your forearm. The heat will gradually increase from a base temperature of 32°C to a maximum of 50°C. You will be given a button to press that will instantly stop the rise in temperature when you feel the heat is intolerable. The thermal pain stimulator is designed to cut off at the maximum temperature and does not burn the skin. We will teach you how to evaluate your pain using a standard verbal scale from 0 to 100, where 0 means no pain and 100 means the worst possible pain.
- Safety event assessment.

You will be closely monitored after methadone administration for the remainder of the study day. After the inpatient visit, participants should be transported home by a person previously arranged by the participant. You will be discharged from DEPRU the following afternoon. You should not drive yourself home. You will need to plan for someone to drive you home following discharge.

Study Day 2 (48 hours after dose) and Study Day 3 (72 hours after dose).
You will be asked to return to DEPRU and the following will occur:

- Review of your current/recent medications.
- Vital signs which include heart rate, blood pressure, breathing rate, carbon dioxide concentration, and measurement of your oxygen levels using a pulse oximeter on your finger.

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- PK blood samples will be collected to measure the amount of study drug in your blood. Blood will be collected venipuncture.
- Pupil size will be measured using a goggle-based, camera-like device.
- You will be assessed on how sleepy or alert you are using a score of 0-5, 0 being asleep and unresponsive and 5 being very alert.
- Self-assessment of methadone effect, will be conducted using the Visual Analog Scale (VAS) This assessment will use a scale from 0 to 100 to rate different factors such as sleepiness, energy level, clumsiness, confusion, anxiety, and nausea.
- We will measure how sensitive you are to pain by using a thermal stimulator. This device applies heat to your forearm. The heat will gradually increase from a base temperature of 32°C to a maximum of 50°C. You will be given a button to press that will instantly stop the rise in temperature when you feel the heat is intolerable. The thermal pain stimulator is designed to cut off at the maximum temperature and does not burn the skin. We will teach you how to evaluate your pain using a standard verbal scale from 0 to 100, where 0 means no pain and 100 means the worst possible pain.
- Safety event assessment.

Study Day 4 (96 hours post-dose) Final Study Visit
After all samples and assessments listed below have been completed, you will have completed the study.

- Review of your current/recent medications.
- Vital signs which include heart rate, blood pressure, breathing rate, carbon dioxide concentration, and measurement of your oxygen levels using a pulse oximeter on your finger.
- PK blood samples will be collected to measure the amount of study drug in your blood. Blood will be collected by venipuncture.
- Pupil size will be measured using a goggle-based, camera-like device
- You will be assessed on how sleepy or alert you are using a score of 0-5, 0 being asleep and unresponsive and 5 being very alert.
- Self-Assessment of methadone effect, will be conducted using the Visual Analog Scale (VAS) This assessment will use a scale from 0 to 100 to rate different factors such as sleepiness, energy level, clumsiness, confusion, anxiety, and nausea.
- We will measure how sensitive you are to pain by using a thermal stimulator. This device applies heat to your forearm. The heat will gradually increase from a base temperature of 32°C to a maximum of 50°C. You will be given a button to press that will instantly stop the rise in temperature when you feel the heat is intolerable. The thermal pain stimulator is designed to cut off at the maximum temperature and does not burn the skin. We will teach you how to evaluate your pain using a standard verbal scale from 0 to 100, where 0 means no pain and 100 means the worst possible pain.

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- Electrocardiogram (ECG) to measure the electrical activity of your heart which can tell us if there are any problems with heart rhythm.
- Safety event assessment.

Early Study Withdrawal Visit

- In the event you choose to end your participation in the study early, an early study withdrawal visit will include the following: blood collection by venipuncture to determine the amount of study drug in your body.
- Safety event assessment.

Maximum Blood Collection Volumes

- Throughout the study, the maximum amount of blood that will be taken from you is around 47 mL. That's about the same as 3.2 tablespoons. Each time a PK sample is collected, up to 18 blood samples of 2 mL each can be taken. Additionally, a total of 8 mL of blood will be collected for on-site laboratory tests. This includes 3.5 mL for pregnancy testing and 4.5 mL for comprehensive metabolic panel (CMP) testing. This total volume also includes a small amount of additional blood (3ml) that is discarded prior to collecting each PK sample.

HOW LONG WILL I BE IN THIS STUDY?
Your participation in the study is expected to last 4 days. A screening visit will occur up to 30 days before active participation in the study.

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.

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WHAT ARE THE RISKS OF THE STUDY?

Risks of methadone
Methadone is a synthetic opioid, which has characteristics typical of opioids. Methadone may cause some, all, or none of the side effects listed below.

- More common:
  - Mild sedation (being in a relaxed, calm state)
  - Lightheadedness
  - Dizziness
  - Nausea
  - Vomiting
  - Sweating

- Less common:
  - Respiratory depression (a decline in the ability of a person to breathe)
  - Low blood pressure
  - Addiction, abuse, and misuse
  - Neurologic disorders including seizures, withdrawal, and spasm of muscles
  - Low adrenal hormone levels
  - Interactions with central nervous system depressants
  - Serotonin syndrome, which is when there's too much serotonin in the brain due to certain medications. It can cause symptoms like restlessness, fast heartbeat, sweating, shaking, and stomach problems).

Respiratory arrest, shock, cardiac arrest, and death have occurred. These risks will be minimized by administering methadone under observation in the inpatient research unit where trained medical personnel are available and there is access to emergency services at all times.

Risks of ondansetron (to help prevent nausea and vomiting**)**

- Headache
- Severe allergic reaction (extremely rare)

Risk of Metoclopramide (to help prevent nausea and vomiting)

- More common:
  - Neurological effects such as dizziness, drowsiness, confusion and difficulty concentrating. These effects are self-limiting and usually resolve within 24 hours of drug discontinuation.
- Less common:

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  - Gastrointestinal effects such as constipation, diarrhea, dry mouth
  - Cardiovascular effects such as high or low blood pressure, a fast or slow heartbeat
  - Mental health effects such as anxiety, depression, irritability or restlessness
  - Sudden, uncontrollable movements of the face, or body that are associated with prolonged use.
- There is a moderate risk of drug-drug interaction with use of metoclopramide in combination with methadone.
  - Metoclopramide has been shown not to work as well when taken together with methadone.
  - The combination of methadone and metoclopramide may increase the risk of dizziness, drowsiness, confusion and difficulty concentrating that can occur with use of methadone.

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

Drug and Food Interactions
For your safety, you must tell the study doctor or nurse about all the prescribed medications, foods, drugs, herbal products, over-the-counter (OTC) medications, vitamins, natural remedies, and alcohol that you are taking before you start the study.

Prescribed medications that affect the body's level of serotonin—like fluoxetine (Prozac), sertraline (Zoloft), and escitalopram (Lexapro)—should not be taken, and use of these medications will not allow you to participate in this study.

Similarly, antidepressants (bupropion) or anti-anxiety medications such as benzodiazepines, muscle relaxants, and other opioids should not be taken, and use of these medications will not allow you to participate in this study.

Also, you may not take medicines that either block or increase the activity of an enzyme called CYP2B6 for 30 days before joining the study or at any time during the study. Taking these kinds of medications will not allow you to participate in this study.

Examples of CYP2B6 inducer medications include: artemisinin antimalarials, barbiturates, carbamazepine, cyclophosphamide, efavirenz, lopinavir, methimazole, nelfinavir, phenobarbital, phenytoin, primidone, rifampicin/rifampin, ritonavir, abacavir, amprenavir, nevirapine, telaprevir.

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Examples of CYP2B6 inhibitor medications include: clopidogrel, prasugrel, thioTEPA, ticlopidine, voriconazole, macrolide antibiotics, azole-antifungal agents, fluconazole, Alstonia boonei, Mangifera indica, and Picralima nitida.

Taking medications such as zidovudine, desipramine or other drugs may increase your body's serum concentration of methadone and it is for this reason you will be asked by site staff if you take these or other drugs that may increase your body's serum concentration of methadone. Taking these kinds of medications will not allow you to participate in this study.

Risks of Pain Sensitivity Testing
Risk of injury with thermal (heat) pain testing is minimal in that this is a widely used and safe procedure. While pain is produced, risk to the individual is minimal, because the pain is brief in nature, can be stopped at any time including at the request of the participant, and generally goes away immediately after the procedure. Similarly, a slight risk of burn is involved using thermal stimuli, although this is a very rare occurrence with the protocol we are using for this study.

Risks of Electrocardiogram (ECG)
Possible side effects of the ECG are skin irritation, itching, and redness from the ECG electrode pads.

Risks of IV Infusion and Taking Blood from IV
The study drug is administered through an IV catheter which is a small, flexible hollow tube inserted into a vein in your arm. Inserting an IV requires a needle and can cause localized discomfort. During IV infusion you are unlikely to feel discomfort. The vein the catheter is inserted in may become inflamed with signs of redness and warmth at or near the IV insertion site. Inflammation in a vein due to a blood clot is also a potential risk. In some instances, the vein may develop a small rupture causing the drug to leak out of the vein. This is generally not dangerous, but can cause discomfort and bruising. There is a risk of infection; however, this is a small risk as aseptic technique will be used. Blood samples will be drawn from your IV. The potential risk related to this are: risk of infection into the bloodstream during blood draw procedure, pain or discomfort, inflammation of the vein known as phlebitis, and bruising at injection site.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there is no direct medical benefit to you. We hope that in the future the information learned from this study will benefit other people.

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What happens to my study data and samples?
The data we record as part of this study will be stored in a secure database. All study data in the database and samples will be given a unique code number and will not be labeled with your name or initials, social security number, address or telephone number. Only the site staff conducting this study at Duke can match your name to this code number, if it is necessary to do so.

After the study is completed, all data and samples are de-identified, meaning anything that could be used to identify you will be removed from the samples and data. All de-identified study data will be submitted to a NIH-designated storage location such as the NICHD Data and Specimen Hub or DASH (https://dash.nichd.nih.gov), or the NIH database of Genotypes and Phenotypes or dbGaP (https://www.ncbi.nlm.nih.gov/gap/). Leftover de-identified study samples will be submitted to an NIH sample storage location. With NIH approval, these data and samples may be used by other researchers in the future. The purpose of sharing this information is to make more research possible that may improve people's health. This will be done without obtaining additional permission from you.

Individual level genomic data will be managed in a controlled-access manner. Controlled access means that only researchers who apply for and get permission to use the information and samples for a specific research project will be able to access the information. Other researchers may conduct whole genome sequencing (WGS) in the future. By doing WGS, the other researchers may have information that is unique to you.

The data and samples collected in this study may be kept forever. We may publish the results of this study. However, we will not include you or your name or any other identifying information.

What information will be in my records at the study location?
Study data entered in your medical records will be kept per Duke's policies. Other study records will be kept until the FDA has completed their review of the results or for a minimum of 2 years after the study has ended, whichever is longer. A copy of this signed form may go into your medical record. This will allow the health care providers caring for you to know what tests you are receiving as part of the study and to know how to take care of you if you have other health problems or needs during the study. It is possible that you may not be able to see the information that has become part of your medical record until the entire study is over.

HIPAA
The United States government has a Privacy Rule to protect the privacy rights of patients. The Privacy Rule protects the confidentiality of personal health information that can be linked to a specific individual. The information protected under the Privacy Rule is often referred to as "protected health information" or PHI. This section, called an "Authorization," explains how your PHI will be used and shared, and it also describes your rights.

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Your PHI, which may include your dosing information and the results of any tests, therapies, or procedures that you have had for your medical care will be shared by site staff with individuals and organizations that oversee this study, including:

- The study team (named on the first page of this form), and their authorized representatives, including laboratories that may be hired to perform tests,
- Government agencies, such as the U.S. FDA and NICHD, a part of the NIH, who will obtain information from this study under the data collection authority given to them under U.S. law.
- The Institutional Review Board (IRB) that reviews the ethical conduct of this study

We try to make sure that everyone who sees your PHI keeps it private, but we cannot guarantee this. If your information is shared with anyone outside the study team, it may be further shared by them and may not be covered by federal privacy laws. Except when required by law, we will only use or share Information outside the study team in a way that nobody can tell it is your information.

There is no expiration date for the use of this information as stated in this Authorization, but you have the right to stop this Authorization at any time.

Will I see any study results?
We will not share the study results with you. However, if any general health or drug screening issues are detected during lab collection, we will share those results. Additionally, for women, the outcome of a pregnancy test will be shared if it is positive.

We may also publish a summary of the results on the following website in the future: www.pediatrictrials.org.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);

2) you have consented to the disclosure, including for your medical treatment; or

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3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the Food and Drug Administration (FDA).

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy. Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

WHAT ARE THE COSTS TO YOU?
There will be no cost to you associated with taking part in this study.

WHAT ABOUT COMPENSATION?
You will be compensated up to $800 for your expenses related to your participation (e.g. parking, gas, and time). This includes $100 for the screening visit, $400 for inpatient visit (Day 0-1), and $100 for each follow-up visit (Day 2, Day 3, and Day 4). Participants who live greater than 50 miles away from DEPRU may qualify for limited reimbursement for transportation and hotel expenses with proper documentation (receipts) and prior authorization by study team. If you withdraw from the study early, you will still receive compensation for the parts of the study you have completed.

Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual totals $600 or more in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University adding up to $600 or more during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by National Institute of Child Health and Human Development (NICHD), Duke University, Duke University Health System, Inc., or your Duke physicians to provide any reimbursement or payment to you in the event of a study-related injury.

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For questions about the study or research-related injury, contact Dr. Shruti Raja at 919-684-1672 during regular business hours and for after hours and on weekends and holidays please page at 919-970-8803.

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 side effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

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 at Duke.
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 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. Reasons why this might occur include because the sponsor decided to stop the study overall. If this occurs, you will be notified and your study doctor will discuss other options with you.

A description of this clinical trial will be available on https://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.

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 Dr. Shruti Raja. For questions about the study or research-related injury, contact Dr. Shruti Raja at 919-684-1672 during regular business hours and at 919-970-8803 after hours and on weekends and holidays.

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 the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

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IRB No: Pro00106216 **DEPRU No:** NL01 **Protocol No:** NL01-MTD

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

_____
Printed Name of Subject

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____
Printed Name of Person Obtaining Consent

Subject Initials _____