Cover page

Title: Neuromodulation Using Vagus Nerve Stimulation Following Ischemic Stroke as Therapeutic Adjunct (NUVISTA)

NCT number: NCT05390580, **Approval Date:** 2/4/2025

Study Title: Vagus Nerve Stimulation following a Large Vessel Occlusion Acute Ischemic Stroke (NUVISTA)

Principal Investigator: Osvaldo J. Laurido-Soto MD

Co-investigator(s): Jin-Moo Lee MD, PhD; Eric C. Leuthardt MD

Sponsor or funding source: None

Objectives

To quantify inflammatory markers in the blood of patients who present with ischemic strokes due to large vessel occlusions to Barnes Jewish Hospital, and determine if treatment with auricular transcutaneous vagal nerve stimulation alters the levels of inflammatory markers in these patients over time, and we will explore if it impacts their overall outcome.

Methods and Measures

Design

This is a randomized open-label, with blinded outcome pilot study to evaluate the effect on inflammatory laboratory values and explore clinical outcomes in patients who present with ischemic strokes due to large vessel occlusions and are treated with either current accepted management, or accepted management in addition to transcutaneous auricular vagal nerve stimulation.

Setting

Patients in this study will be inpatient at Barnes Jewish Hospital

Data Collection Criteria

Adult patients who present with acute ischemic strokes due to large vessel occlusions to Barnes Jewish Hospital will be considered for enrollment in this study. Exclusion criteria will include patients <18 years old, patients with presumed chronic large vessel occlusions, posterior circulation LVOs, NIHSS<6, CTP Penumbra <1/3 total ischemic area, pre-morbid modified Rankin score (mRS) >2, unable to initiate treatment under 36 hours from symptom discovery, life expectancy <3 months, patients' undergoing active cancer or immunosuppressive/modulating therapy, or patients with sustained bradycardia on arrival with a heart rate <50 beats per minute.

Sample size

We anticipate enrolling approximately 80 patients into the study, with random assortment to treatment with standard medical care, and standard medical care with transcutaneous auricular vagal nerve stimulation.

Intervention

Patients enrolled in the trial will be randomized to treatment with or without electrical stimulation via an auricular, transcutaneous vagus nerve stimulator. All patients will be fitted with the device, we will attach adhesive contacts to the left ear. Stimulation sessions will occur for 20 minutes twice daily during the inpatient period. Patients assigned to the controls arm will have no electricity applied,

those treated with stimulation will be treated with the following parameters: frequency 20 Hz, pulse width 250 μm, and varying intensities from 0.4 mA to 2 mA (intensity is always titrated to be a level below painful threshold in a patient). The amplitude of stimulation may be reduced if a patient complains of discomfort at the site of stimulation. The site of stimulation will be inspected daily before and after treatment to ensure there is no redness or irritation at the site.

Outcome Measure(s)

The primary endpoints of the study will be changes in the levels of inflammatory markers that include IL-1b, IL-6, TNF-α, and white blood cell count in the blood, as well as specific inflammatory cell counts (neutrophil to lymphocyte ratio, for example) at time of admission, and every day throughout the hospitalization. The secondary exploratory endpoints will be clinical outcomes assessed via the change in daily NIHSS and mRS at 30 and 90 days, as well as safety endpoints with regards to blood pressure and heart rate. We will also do mononuclear cell genetic testing to attempt to identify phenotypes that respond to the intervention. Follow up data will be obtained via chart review, we will obtain the mRS data at 30 days over the phone, and we will make additional outpatient follow up appointments for the research study in order to collect the NIHSS and mRS data at 90 days.

Analytical Plan

Results will be analyzed initially using descriptive statistics. Comparison between groups will be done using chi square tests for proportions, and t-tests or ANOVA procedures for continuous variables. Regression analysis will be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate. Please see document with statistical plan that is attached.

Human Subjects Protection

Subject Recruitment Methods

Intensive care unit staff as well as physicians in the Department of Neurology will be made aware of this study, and be directed to notify the research group when a patient presents with an ischemic stroke due to a large vessel occlusion. The research team will then screen the patients to see if they are eligible for enrollment in the study. Additional patient data, including medical history, laboratory values, and clinical assessments will be obtained from the electronic health records.

Informed Consent

Informed consent will be obtained from the patient if they are able, or from the appropriate party that is providing consent for their medical care if they are unable to provide consent. A copy of the paper consent is also submitted.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, and maintaining all study information in a secure manner. Data will be de-identified and stored with an assigned ID number. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

Abbreviations:

ANOVA: Analysis of variance

AIS: Acute Ischemic Stroke

CRP: C-Reactive Protein

CT: Computerized Tomography

ID: Identification Number

IFN: Interferon

IL: Interleukin

LVO: Large Vessel Occlusion

MRI: Magnetic Resonance Imaging

NIHSS: National Institute of Health Stroke Scale

TAVNS: transcutaneous auricular Vagal Nerve Stimulator

TGF: Transforming growth factor

TNF: Tumor Necrosis Factor

VNS: Vagal Nerver Stimulator

Expanded Statistical Analysis:

Statistical analysis.

Statistical analyses were performed using Stata/MP version 18 (StataCorp LLC 2023, Statistical Software, College Station, TX) and Python packages Scipy and Statsmodels. All continuous variables were retained as continuous, except where noted. Multivariable regression was used to examine treatment group associations with outcomes, except for rare secondary outcomes/adverse effects. Following FDA recommendations, an intention-to-treat (ITT) approach was implemented. Primary ITT analyses were conducted without transformation of continuous outcome variables because ≥35 observations were available.

Statistical analysis of rate of change in cytokines, WBC, and neurological outcomes in taVNS vs. sham treatment.

Longitudinal data were analyzed using mixed effects models per the FDA, with person as a random effect, given multiple records per person. For cytokine models, assay plate was included as an additional random effect. This approach accommodated irregularly timed points, less restrictive missing data assumptions, and time-varying variables. To complement our primary ITT approach, treatment also was handled as time-varying when noted, with assignment occurring at randomization. All longitudinal models included treatment, time since LKN, and their interaction term(s) as primary independent variables to test whether the pattern of change over time differed between the taVNS and sham groups. Time was modeled quadratically for cytokine and WBC outcomes to capture the known U-shaped associations with time when modeling these outcomes and linearly for in-hospital NIHSS scores based on panel data plots. For NIHSS, a single model was constructed to estimate the rate of change (change in NIHSS per

day) in each of the two treatment groups and to formally test whether these rates were different. For 30-day NIHSS changes (vs. baseline) and 90-day mRS changes, we used the parallel model, with actual assessment days scaled to standardize the evaluation period to 30 or 90 days, respectively. We characterized the daily change in each WBC or cytokine outcome using a similar model expanded to include the quadratic terms. Treatment-time interactions were tested using likelihood ratio tests comparing models with and without interaction term (NIHSS, mRS) or terms (cytokines, WBC), with significance at two-sided $\alpha=0.05$. These analyses were adjusted for baseline covariates, including baseline NIHSS (except in NIHSS models, which included this observation), time from LKN to thrombus removal time or recanalization attempt (groin puncture time), and percent reperfusion (0-100%) based on TICI score to obtain a single semi-continuous measure. In sensitivity analyses, we also performed the analysis with a dichotomized TICI scale (reperfused ≥2B, not reperfused <2B) or restricted data to the first five days post-LKN (when most stimulations and hospitalizations had ended). Finally, we explored whether any difference in longitudinal patterns between taVNS and sham depended any of the *a priori* adjustment variables, i.e., whether any time-treatment interaction depended on one of these three variables. We conducted post-hoc t-tests to compare cytokine levels between groups on each day.

Statistical analysis of safety and exploratory analysis of the Stroke Complications and Poor Outcomes in relation to treatment.

To assess our dichotomous safety endpoints, we used logistic regression models constructed to assess differences in bradycardia, hypotension, infection, hemicraniectomy, hemorrhagic transformation, and deaths amongst treated vs non-treated patients. To explore the hypothesis that taVNS reduces the incidence of complications and poor outcomes, we performed logistic

regression models for discharge related outcomes, defined as: readmission, length of stay, and hospital poor disposition (i.e. nursing home, long-term acute care hospital, or death).

Washington University in St. Louis

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IRB ID #: 202203086
APPROVAL DATE: 02/04/25
RELEASED DATE: 02/05/25
EXPIRATION DATE: 02/03/26

INFORMED CONSENT DOCUMENT

Project Title: Neuromodulation Using Vagus Nerve Stimulation Following Ischemic Stroke as Therapeutic Adjunct (NUVISTA)

Principal Investigator: Osvaldo Laurido-Soto, MD

Research Team Contact: Osvaldo Laurido-Soto, MD
Email: ojlaurido-soto@wustl.edu
Work Phone: 314-273-3294

If you are the legally authorized representative providing consent the word "you" in this document refers to the person you represent.

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you have presented to the hospital with an acute ischemic stroke due to a large vessel occlusion. An acute ischemic stroke due to a large vessel occlusion is a clot inside the head in one of the main vessels/arteries in the brain. It can occur for many reasons, which include: age, high blood pressure, diabetes, bad cholesterol, and potential heart irregular rhythms, among others.

The purpose of this research study is to better understand the role of inflammation in recovery from an acute ischemic stroke, and to see if electrical stimulation to the ear can improve outcomes. Previous research has shown that the inflammation markers in our blood increase after an acute ischemic stroke, and that this inflammation may lead to worse outcomes. Stimulating the vagus nerve, which has a branch that runs in the outer ear, has been shown to reduce inflammation in the body. Our team wants to measure your inflammatory markers throughout your hospital stay, and provide either the current standard medical therapy or daily ear stimulation in addition to current standard medical therapy to determine if there is a difference in recovery. If you are assigned to the stimulation arm of this study, you will have a daily electrical stimulation applied to your vagus nerve through a device placed on your ear for five days. You may also be assigned to a "control" group. If you are assigned to the "control" group, you will still be fitted with the device, but no electrical current will be applied through the device.

Auricular transcutaneous vagus nerve stimulation is approved by the U.S. Food and Drug Administration for epilepsy, refractory depression, and obesity. However, the use of auricular transcutaneous vagus nerve stimulation is considered investigational in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

Following enrollment in the study, your medical record will be reviewed to obtain some important details about your acute ischemic stroke, and your medical history prior to this hospitalization. The details recorded by the research team will include the severity of your stroke (both based on your imaging and your physical exam on arrival to the hospital). It will also include information about the location of the occlusion that is identified on your imaging, how much brain tissue is damaged and at risk, and how you are treated during your hospital stay. With regards to your medical history, the research team will review the medical record and document your medical history. The research team will also review your medications you take at home.

Laboratory Studies

Initial lab work already obtained by the intensive care or progressive care unit team will be reviewed. Additional blood samples will also be taken to measure the level of several inflammatory markers on the first day of enrollment. This blood work will be repeated approximately every 2 days during the course of your hospital stay. This blood work may require a needle stick, similar to how other blood samples are drawn, or may be sampled from a line already in place without a new stick. Each set of lab draws will require approximately 2 teaspoon of volume, and the total volume required will depend on the duration of your hospital stay. For example, if you are in the hospital for 5 days, a total of 24 cc blood will be collected over this time period. For some patients, additional blood tests may be drawn a second time on these days after treatment with ear stimulation. Therefore, the total volume over the duration of hospitalization would be higher but less than 10 to 12 teaspoons of blood over 2 weeks. There is a possibility that you may also be enrolled on an observational study called “MAESTRO”, IRB# 202110028. If blood was already drawn for this study we might share the blood samples instead of drawing new blood.

Genetic Research

Genes are a unique combination of molecules (called DNA) that we inherit from our parents. There are millions of tiny differences in our genes. These differences may make us more or less likely to develop certain diseases or conditions or to have certain characteristics. Genetic research involves studying the differences in genes and DNA between individuals. This type of testing creates information that is as unique to you as your fingerprint.

We will study the relationship of your genes to your response to the intervention with the auricular transcutaneous vagus nerve stimulation and see if this is related to a difference in stroke size and functional recovery.

Ear Stimulation

You will be randomly assigned to treatment with electrical stimulation to different parts of the ear. Electrical stimulation to the part of the Ear that has the branch of the vagus nerve (intervention) or the part that has the great auricular nerve (sham).. This means that the part of the ear to be treated will be determined purely by chance, like flipping a coin. You will have a 50/50 chance of being in any one of the study groups. You will be “blinded”, which means you will not know which of these groups you are

assigned to.

The device that will provide stimulation is the transcutaneous auricular Vagus Nerve Stimulation (taVNS) device by Sotarix Medical©. It is a portable transcutaneous electrical nerve stimulation unit. This small device is connected to the ear with adhesives, which will be applied to the left ear during the treatment periods. The treatment period with the device will last 20 minutes, and will occur twice each day during your stay in the hospital. The most common negative side effect of the stimulation is redness or irritation at the site, although this is uncommon with the length and amount of stimulation we will use. Our team will be trained to provide the stimulation and inspect the area of stimulation daily to ensure there is no redness or irritation. Further stimulation will not be applied if irritation is noted.

Before, during, and after the ear stimulation your vital signs (like your heart rate, and your blood pressure) will be monitored and recorded. Monitoring devices will already be in place while you are in the Intensive Care Unit or Neurological Care Unit, and this study will not require any new monitoring devices to collect this information.

This stimulation device is FDA approved for the treatment of epilepsy (seizures), depression, and obesity, but is not approved for the treatment of subarachnoid hemorrhage.

Follow-up

You will be required to attend a follow up appointment at 30 days following your discharge from the hospital (or longer depending on physician availability). This follow up appointment will be either in-person, by phone, or via telemedicine. This will be either your normal scheduled visit if it is at 30 days or a scheduled appointment coordinated by us. If it is a scheduled appointment coordinated by us outside standard of care, you will be eligible for $25 compensation in the form of a gift card. You are eligible for a $50 check payment upon completion of this initial follow up visit. The check will be mailed to your home address upon completion of the visit. You will also be required to participate in a brief telephone call at 90 days to assess your functional status. The research team will review the normally scheduled visits you attend following your hospitalization to better understand the long-term impact of the stimulation on outcomes. The information obtained will include disability assessment results, and physical exams performed. The study team will continue to access these records for up to two years following your initial hospitalization.

Will you save my research information to use in future research studies?

We would like to use the data we are obtaining in this study for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding acute ischemic strokes due to large vessel occlusion, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data you give up any property rights you may have in the data.

Your data will be stored without your name or any other kind of link that would enable us to identify

which sample(s) or data are yours. Therefore, it will be available for use in future research studies indefinitely and cannot be removed.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 80 people will take part in this study conducted by investigators at Washington University

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for the duration of your hospitalization, and any follow-up appointments that occur in the 2 years following your hospitalization for your acute ischemic stroke.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Likely / Common

- None

Less Likely / Less Common

Life Threatening

- None

Serious

- None

Mild

- Skin irritation/redness at the site of stimulation

Rare

Life Threatening

- None

Serious

- Bradycardia (slow heart rate)
- Hypotension (low blood pressure)

Mild

- Discomfort or pain during the stimulation period

Blood Drawing
The blood draw may cause bleeding, bruising, or pain. Some people become dizzy or feel faint. There is also a rare risk of infection.

Risks of Genetic Research

There may be information obtained from the genetic testing that indicates that you, or potentially a family member (since we inherit genes from our parents, and pass genes on to our children) are at risk for a particular disease or condition. For example, genetic sequencing may indicate that an individual is more prone to develop certain types of cancer or other types of diseases, (e.g. Alzheimer's or other inherited diseases).

If made available to persons or agencies outside of our research group, information about genetic test results could affect your employment or insurance. For instance, employers, insurers, or others may use this information when making decisions about you or your family members regarding employment, insurance, or other benefits.

While the data developed for this study is being stored without traditional identifiers (stored only with coded ID numbers, no names), there may be ways of linking the genetic materials back to you. Because your DNA is unique to you, it is possible that someone could look at the information in the DNA database and compare it to information in another database, and use that to identify you. This is difficult to do and is very unlikely to happen.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long term-care insurance.

Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure, and we think the risk of accidental disclosure is very small. Please see the section in this consent form titled "*How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because it could give us new treatment strategies for acute ischemic strokes due to large vessel occlusion.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could receive the currently accepted standard care for acute ischemic stroke alone. Please note, the addition of treatment with the vagus nerve stimulator

does not prevent you from receiving all of the normally available and recommended medications and therapies currently used for subarachnoid hemorrhage.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any additional costs for being in this research study. You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You may be paid for being in this research study. You are eligible for a $50 check payment upon completion of in-hospital interventions. This check will be mailed to your home address after the in-hospital interventions have been completed. You are also eligible for $50 check payment upon completion of your first follow up visit after your discharge from the hospital. This check will be mailed to your home address after the first follow up visit after your discharge has been completed.

You will be asked to provide your social security number (SSN). You may also need to provide your address if a check will be mailed to you. You should receive payment between 3 and 6 weeks upon completion of the follow-up study visit If a follow-up appointment is scheduled by us outside standard of care, you will be eligible for $25 compensation in the form of a gift card.

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at 314-296-0016 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University**.** If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration

- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, we will limit access to your personal health information to the fewest number of necessary researchers. We will use a de-identified method of recording your data, so that your name or other identifiers are not linked with the collected data. We will also implement the use of encrypted devices for storage of all data.

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.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- Your treatment or the care given by your health provider.
- Your insurance payment or enrollment in any health plans.
- Any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
    - **If you revoke your authorization:**
      - The research team may only use and share information already collected for the study.
      - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because it is considered unsafe for you to continue in the study, because funding for the study has ended, or because the sponsor has decided to stop the research project.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Osvaldo Laurido-Soto, MD at 314-273-3294. If you experience a research-related injury, please contact: Osvaldo Laurido-Soto, MD at 314-273-3294.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 02/03/26.

_____ _____

(Signature of Participant) (Date)

_____
(Participant's name – printed)

Legally Authorized Representative's Name and Relationship to Participant:

Do not sign this form if today's date is after **EXPIRATION DATE: 02/03/26.**

_____
(Participant's name – printed)

_____ _____
(Signature of Legally Authorized Representative) (Date)

_____ _____
(Name of Legally Authorized Representative – printed) (Relationship to Participant – printed)

Who should sign as the Legally Authorized Representative (LAR)?
If the participant has a legal guardian or attorney-in-fact this individual must sign as the LAR.

If there is no legal guardian or attorney-in-fact the individuals listed below may sign in order of priority.

(1) Spouse unless the participant has no spouse, or is separated, or the spouse is physically or mentally incapable of giving consent, or the spouse's whereabouts is unknown or the spouse is overseas;
(2) Adult child;
(3) Parent;
(4) Brother or sister;
(5) Relative by blood or marriage.

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)