Institutional Review Board
Informed Consent Document for Research
MASTER CONSENT

Study Title: Trial of Early Antiviral Therapies during Non-hospitalized Outpatient Window (TREAT NOW) for COVID-19
Version Date: October 30, 2020

Part 1 of 2: MASTER CONSENT

Name of participant:_____Age: _____

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
You are being asked to take part in this research study because you tested positive for SARS Coronavirus 2 (SARS-CoV-2), which leads to Coronavirus Disease 2019 (COVID-19), and you do not need to be in the hospital. This study will enroll up to 600 people.

The symptoms may include fever, cough, shortness of breath or other cold or flu-like symptoms, which may appear 2-14 days after exposure. **If you develop trouble breathing, persistent pain or pressure in the chest, new confusion or trouble waking up or bluish lips or face, get medical attention immediately.**

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, more serious illness can occur in any person with COVID-19 and lead to hospitalization. Older people and people of all ages with severe chronic medical conditions like heart disease, lung disease and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

The purpose of this study is to collect information needed to understand if a potential treatment, lopinavir/ritonavir, could possibly help people recover faster and/or prevent serious events such as hospitalization or death. We do not know if the study drug will make COVID-19 better or worse or have no effect.

If you agree to be in the study, you will be in the study for about 30 days and will take study drug for 14 days.

Although this study is short, we don't want to enroll participants who may be pregnant, become pregnant, or breastfeed.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

This study is randomized, blinded, and placebo-controlled, which means that you will either receive lopinavir/ritonavir or placebo. A placebo is made to look like the study drug tablet but does not have any study drug in it. Researchers use a placebo to see if the study drug works better or is safer than not taking any active medication. Randomized means that no one can choose who receives the study drug and who receives the placebo. It is up to chance. You have a one in two chance of receiving lopinavir/ritonavir or placebo. Blinded means that you, the study doctor and the study team will not know which tablet you receive.

Lopinavir/ritonavir is an FDA approved drug used in HIV-1 patients to slow the progression of the HIV-1 virus. Laboratory tests and some early human studies suggest it may have activity to fight the SARS-CoV-2 virus.

In this study, lopinavir/ritonavir is considered investigational, which means ithasnot been approved by the U.S. Food and Drug Administration (FDA) for use in COVID-19.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told, so that you can decide whether or not you still want to be in this study.

Side effects and risks that you can expect if you take part in this study:

Risks of Lopinavir/Ritonavir:
General Risks
The most common side effects were diarrhea (loose stools), nausea (feeling sick to your stomach),

vomiting, hypertriglyceridemia (Increased blood level of a form of fat called triglyceride), and hypercholesterolemia (Increased blood cholesterol level). Diarrhea, nausea, and vomiting occurred more often at the start of therapy while hypertriglyceridemia and hypercholesterolemia generally occurred later. Diarrhea was reported more often when this drug was used once a day than when it was used twice a day. In this study the study drug is taken twice a day.

The very common side effects (10% or more) are:

- Diarrhea (loose stools)
- Nausea (feeling sick to your stomach)
- Hypertriglyceridemia (Increased blood level of a form of fat called triglyceride)
- Increased total blood cholesterol level
- Hypercholesterolemia (Increased blood cholesterol level)
- Upper Respiratory Infection (upper lung infection)

The most common side effects (less than 10%) are:

- Vomiting
- Abdominal Pain (stomach pain)
- Dyspepsia (heartburn)
- Gastroesophageal Reflux Disease (chronic heartburn and indigestion)
- Flatulence (gas)
- Headache (pain in the head, including migraine)
- Dizziness or drowsiness (feeling faint or tired)
- Pancreatitis (inflammation of the pancreas causing stomach pain) Pancreatitis should be considered if clinical symptoms (nausea, vomiting, abdominal pain)
- Hepatotoxicity (damage to the liver)
- Lower Respiratory Infection (lower lung infection)
- Hemorrhoids (a condition that affects the vessels located around the anal area)
- Gastroenteritis and Colitis (inflammation of the stomach and/or intestines
- Blood Glucose Disorders (including diabetes mellitus)
- Musculoskeletal pain [muscle pain including arthralgia (joint pain), back pain]
- Peripheral Neuropathy [nerve damage (possible numbness, pain, and/or loss of motor function)]
- Neutropenia (low white blood cell count which increases your risk of infection)
- Lymphadenopathy (lymph node swelling)
- Anxiety (feeling of fear, worry, and uneasiness)
- Insomnia (difficulty sleeping or falling asleep)
- Cellulitis (an infection of the skin)
- Dermatitis/Rash (including eczema, seborrheic dermatitis),

- Night sweats
- Pruritus (itchy skin)
- Cerebrovascular Accident (stroke)
- Erectile dysfunction
- Menstrual Disorders (amenorrhea, menorrhagia)

Uncommon (1% or less)

- Stomatitis and oral ulcers (sores in the mouth and esophagus, which may be painful and cause difficulty swallowing)
- Duodenitis or Gastritis (inflammation of the intestines and/or stomach)
- Gastrointestinal Hemorrhage (bleeding of the stomach and/or intestines)
- Fecal incontinence (inability to control bowel movements)
- Lactic Acidosis (abnormal blood acid/base balance)
- Hyperbilirubinemia (abnormally high levels of bilirubin in the blood)
- Osteonecrosis (bone destruction)
- Tinnitus (ringing in the ears)
- Hemolytic Anemia (anemia due to destruction of red blood cells)
- Hematuria (blood in the urine)
- Alopecia (hair loss)
- Vasculitis (blood vessel inflammation)
- Deep vein thrombosis [blood clots in a vein (possible pain, swelling, and/or redness)]

Frequency not reported

- Dysphagia (difficulty swallowing)
- Eructation (burping)
- Esophagitis (inflammation, irritation or swelling of the esophagus)
- Dehydration (Excessive loss of body water)
- Cholecystitis (an infection of the gallbladder)
- Dyspnea (shortness of breath)
- Pulmonary Edema [fluid in the lung (possible difficulty breathing)]
- Pharyngitis (sore throat)

Sometimes liver tests are done before starting lopinavir/ritonavir for long term use, but given the quarantine that you are being asked to abide by for your COVID and the short duration of treatment being used, it is thought to be safe to give this short treatment course without doing these tests first.

Risks that are not known:
Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not

know about at this time.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study:

- May help develop important scientific knowledge that could contribute to the development of a treatment for patients with COVID-19 and other COVID-like illnesses.

Procedures to be followed:
Screening/Randomization
The study team will review your medical record

- To confirm a positive SAR-CoV-2 test result
- To confirm your medications and medical history and review any available electrocardiograms to determine if you are potentially eligible to take part in this study.

The study team will contact you to explain:

- The study and what will be required of you.
- Review all medications you are taking including prescription medications, over the counter medications and supplements.
- Ask you general information about yourself including race, ethnicity, and gender.
- We will ask you for an alternate contact who can answer questions about you.
- We ask you questions about your medical history.
- Review the remote consent process. The study team will answer all your questions. You will be able to ask any questions that you might have. If you want to take part in this study, you will complete the remote consent process.

After you have provided consent and once you are determined to be eligible to take part in this study:

- You will be randomized to either lopinavir/ritonavir or placebo.
- The study team will review your shipping address and study drug will be shipped to you by overnight mail.

Days 1 thru 29
You will take the study drug twice a day for 14 days. You will complete an electronic daily symptom survey or answer questions over the phone about how you are feeling, and we will ask about any new medications. We may call and remind you to complete the electronic surveys. If you are unable to complete the daily symptom survey electronically, the study team may call you to ask you these survey

questions over the telephone. We may also call you to ask more questions about your responses or if you request that we call you. We also collect information about how you are doing around Day 29.

If you become hospitalized – we may also call your study doctors to see how you are doing. We will ask you to sign a release of information so that we may obtain your medical records if you become hospitalized. We will also ask you for alternative contacts so that we may contact others to see how you are doing if you do not answer the questions. If you are hospitalized prior to completion of the study medication, an attempt will be made to continue study medication.

If we are unable to reach you by phone, we will contact the alternate contact you have provided to obtain information about you.

Reasons why the study doctor may take you out of this study:
The study doctor may take you out of the study if he or she thinks it is not in your best interest. If the sponsor stops the study, you will be taken out of study. If you are taken out of this study, you will be told the reason why.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry.
A description of this clinical trial will be available on 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 Web site at any time.

Privacy:
Any information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the data collected. This data may help us, or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your study data may be used to make new products or tests. This data may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you.

Study Results:

Study results will not be shared directly with participants but will be available through www.clinicaltrials.gov and publication in medical journals.

Part 2 of 2: STUDY SITE INFORMATION

Site Name:	Vanderbilt University Medical Center
Site Principal Investigator:	Todd W. Rice, M.D., MSc.
Site Principal Investigator Contact:	615-322-3412
Site Study Coordinator:	Margaret Hays, RN, MSN, CCNS
Site Study Coordinator Contact:	615-343-8013

This part of the consent form includes information about the site that is asking you to participate in this study and is specific to participation at your site only. Before making your decision, both the site-specific information and the general study information should be reviewed with you. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Payments for your time spent taking part in this study or expenses:
You will be paid one $50.00 pre-paid gift card or check for completing the daily surveys.

Costs to you if you take part in this study:
There is no cost to you for taking part in this study.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Todd Rice, MD at 615-322-3412.
For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Medical Center Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us, or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

Confidentiality:
Vanderbilt University Medical Center may share your information and/or samples, without identifiers, to others or use it for other research projects not listed in this form. The sponsor, Vanderbilt University Medical Center, Dr. Rice and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

You will not be identified by name in any published reports about this study or in any other scientific publication or presentation.

There is a risk that if people outside the study get your health data, they could misuse it for purposes other than those outlined in this consent. The study team has strict privacy and confidentiality protection procedures in place to prevent this from occurring so the chance of this happening to you is extremely small.

Authorization to Use/Disclose Protected Health Information
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

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How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally.
All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Participant

Participant's Name (print): _____

Signature (if able to consent): _____ Date:____/_____/ ____

Witness

(If Required) Witness's Name(print): _____

Signature (if able to consent): _____ Date:____/_____/ ____

Witness to: □ Discussion □ Signature

Date of IRB Approval: 03/11/2021
Date of Expiration: 01/20/2022

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Study Representative Statement

I have explained the purpose of the research, the study procedures, the possible risks and discomforts, the possible benefits, and have answered all questions to the best of my ability.

Study Representative's Name (print): _____

Signature: _____ Date: ____/____/____

Time Consent Obtained_____:_____AM / PM

You will receive a copy of this form after it has been signed and dated.