

Informed Consent Document

Trial of Early Antiviral Therapies during Non-hospitalized Outpatient Window (TREAT NOW) for  
COVID-19

NCT04372628

January 21, 2021

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Informed Consent Document for Research  
MASTER CONSENT

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**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.

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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 it has not 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),

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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),

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- 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)
- Eruption (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

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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

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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](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 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:**

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Study results will not be shared directly with participants but will be available through [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and publication in medical journals.

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