RESEARCH CONSENT FORM
An Open Label Phase 1 Trial of Losartan for Worsening Respiratory Illness in COVID-19
Protocol # Losartan COVID-19

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This research study will take place at the University of Kansas Medical Center (KUMC) with Dr. Salathe as the researcher. About 50 people will be in the study at KUMC.

Why is this study being done?

Coronavirus COVID-19, caused by the coronavirus SARS-CoV-2 has reached pandemic status. COVID-19 is a respiratory disease, with known symptoms of fever, cough, shortness of breath, respiratory failure, and even death. Older people and people of all ages with severe chronic medical conditions, such as heart disease, lung disease, and diabetes, have an increased risk of contracting COVID-19. Worldwide, there are over 100,000 confirmed cases with over 4000 deaths, and both numbers are rapidly rising.

Currently there are no U.S. Food and Drug Administration (FDA) approved treatments or vaccines for COVID-19. Trials are currently being conducted using anti-viral drugs, such as Remdesivir and Chloroquine to treat COVID-19 symptoms, but additional safe and non-toxic treatment options are needed to prevent the progression of respiratory failure.

By doing this study, we hope to learn if an investigational drug, Losartan, can increase respiratory function in patients diagnosed with COVID-19.

What is being tested in this study?

Losartan has been approved by the FDA for the treatment of high blood pressure and to protect kidneys from damage in patients with Diabetes Mellitus. There is evidence that the coronavirus infects cells by binding to a molecule called Angiotensin-converting enzyme 2 (ACE2). By binding to ACE2, it decreases its activity which results in an increase of angiotensin II that can damage the lungs and heart. Losartan blocks the effects of angiotensin II, thereby possibly helping the lungs to improve.

Losartan is considered investigational because it has not been approved by the U.S. Food and Drug Administration (FDA) for the treatment of COVID-19. Investigational products are still being studied to find out what a safe dose is, what the side effects are, and whether or not the drug is effective in the disease being studied.

What will I be asked to do?
Your participation in this study could last up to 14 days. Participation may end sooner, if your condition becomes worse, or you are discharged from the hospital. If you decide to join the study, you will be asked to read and sign this consent form before any study procedures take place. This is considered an open-label study, meaning all patients will receive Losartan.

Day 0: Once you have joined the study, you will be asked to take one, 25mg pill, Losartan each day. Losartan is taken orally (by mouth), with water. If you are unable to take the medication orally, you will be given it through a feeding tube. Procedures completed at Day 0 include:

- Medical History/Current Medications: Researchers will look at your medical records to review your medical health, any medications you have previously taken, and any medications you are currently taking. You will also be asked demographic questions about yourself such as your name, date of birth and race. Researchers will also look at any labs and radiographic images, such as X-Rays or CT scans from your medical records. We will also access the severity of your disease, and monitor your symptoms of respiratory failure.

- Physical Exam/Vital Signs: You will have a physical examination, which will include collecting your height and weight from your medical records. Your vital signs will be taken including your blood pressure, heart rate, breathing rate and temperature.

- Blood Samples: You will also be asked to provide up to about 9 teaspoons of blood, by inserting a needle in a vein in your arm for routine laboratory tests.
    - You will provide about 3 teaspoons at Day 0 and 3 more teaspoons on the day you complete the study. If your day of discharge is changed after sample collection you may be asked to provide an additional 3 teaspoons of blood.
    - A portion of your blood sample will be stored and kept at KUMC for future analysis related to COVID-19. Providing a blood sample for future analysis is required to participate in this study.

- Nasopharyngeal Swab: You will be asked to undergo a swab procedure that goes into your nose to the back of your throat at the beginning and end of the study to measure the amount of SARS-CoV-2 in your airway.

Day 3: The study team will continue to monitor your condition each day, and if your body tolerates the 25 mg dose of the drug, the study doctor will increase your dose of Losartan to one, 50 mg pill, each day, until you have completed your therapy.

If your body is not responding well to the Losartan, or your symptoms become worse, you

will no longer receive Losartan, and you will return to your normal medical care.

Control Group: If you decide you do not want to take Losartan to treat your COVID-19 symptoms, you can still participate in the study. The study team may ask your permission to allow the study doctor to follow your treatment progress, and use your treatment data, without taking the study drug. Allowing your progress and data to be followed is optional. You will not receive Losartan or give a blood sample for research if you choose this option. You will have the ability to choose this option at the end of this consent form.

What are the possible risks or discomforts?
You may have problems because of the drug used in this study or because of the procedures that will be performed during the study. These are called adverse events or side effects. Some may be only an inconvenience, but some may be harmful. There could be side effects of Losartan that are not yet known, or the research may involve risks to you that are currently unforeseeable. It is important that you tell the study team immediately about any side effects or problems you have.

Losartan Risks

Common Side Effects (may occur in up to 2% or more of patients)

- Fatigue
- Dizziness

Rare Side Effects (may occur in up to 2% or less of patients)

- angioedema (swelling under the skin)
- hypotension (low blood pressure)
- renal (kidney) problems or failure
- blood disease (dyscrasias)
- hepatitis
- rhabdomyolysis (muscle damage)

Allergic Reaction Risks

Sometimes, people have serious allergic reactions to drugs. A severe allergic reaction could be life-threatening and may result in death. Symptoms of allergic reactions include:

- Swelling of the mouth, throat or eyes
- Rash
- Difficulty breathing
- Coughing
- Wheezing
- Sudden drop of blood pressure
- Seizures
- Flushing
- A fast pulse
- Sweating

The study team will monitor you for any allergic reaction during your time in the study.

Blood Draw Risks

During the study you will have blood drawn for laboratory tests. The risks of drawing blood from a vein may include bleeding, infection and a slight bruising at the site that is used

for the blood draw. This will be minimized by careful and clean techniques.

Nasopharyngeal Swab Risks
During the study you will undergo nasopharyngeal swabs. The swabs are placed in the nose and are advanced to the back of the throat. This procedure can cause minor discomfort, sneezing, coughing and, rarely, minor nose bleed.

Risks associated with taking Losartan in combination with other drugs
For your safety, tell the investigator or a member of the study team about any drugs you are taking or planning to take, including herbal products, supplements or drugs without a prescription. The study team will tell you if there might be a problem with the drug combination.

Pregnancy Risks
Losartan can cause birth defects or fetal death if taken during the second or third trimester. Losartan may hurt an unborn child or a child who is breast-feeding. You cannot be in this study if you are pregnant or nursing a baby. You cannot be in this study if you are trying to get pregnant. You will have a pregnancy test before the study starts.

There may be pregnancy risks that are not known yet. Though it's unlikely during your participating in this study, you must tell the study doctor right away if you become pregnant.

Are there benefits to being in this study?
Researchers don't know if you will benefit from this study. If the study drug is effective, you may lower your risk of respiratory failure due to COVID-19. Researchers hope that the information from this research study may be useful in the treatment of other patients with COVID-19.

Will it cost anything to be in the study?
The investigational drug, Losartan, will be provided by the research team free of charge. Any additional costs for administering the drug and monitoring its use are considered routine medical care and will be billed to you and your insurance carrier as well as any medical treatments you receive that are not related to the drug.

Your insurance may not cover some or all of the services if you are part of a research study or taking an investigational drug outside of a clinical trial. There is no requirement by CMS (Medicare and Medicaid) to cover services related to investigational drugs and devices outside of a clinical trial. Pre-Certification is not a guarantee of payment and you may want to talk to your insurance company and review your specific benefits and coverage before deciding to use this drug.

You will be responsible for normal co-pays, deductibles, and non-covered services. You can still receive the investigational drug even if your insurance denies coverage of the routine medical services or if you are uninsured. The hospital has a financial assistance program which is available to all patients who qualify.

You can still be in the study even if your insurance denies coverage for your standard of care services or if you are uninsured. The hospital has a financial assistance program which it makes available to all patients who quality. If you do not qualify for financial assistance you will be responsible for all bills. The study staff will be able to provide more information to you.

Will I get paid to participate in the study?
There is no payment for this study. This study includes providing blood samples to the researcher. The specimens will belong to the University of Kansas Medical Center. There are no plans to pay you if new products are developed from research on your specimens.

What happens if I get hurt or sick during the study?
If you have a serious side effect or other problem during this study, you should immediately contact Dr. Salathe at 913-588-6045. For after hours, please page this number: 913-917-8288 (24-hour number) and the coordinator on call will get back to you. Once you dial the pager number and hear a beep tone, please dial your call back number followed by the pound sign (#). You will then hear an automatic message “thank you for calling” confirming page was received. If you don’t receive a prompt response and need medical advice, you should call 913-588-5000 and ask for the pulmonology attending physician on call. Please tell the physician that you are in this research study. A member of the research team will decide what type of treatment, if any, is best for you at that time.

If you have a bodily injury as a result of participating in this study, treatment will be provided for you at the usual charge. Treatment may include first aid, emergency care and follow-up care, as needed. Claims will be submitted to your health insurance policy, your government program, or other third party. You will be billed for the costs that are not covered by the insurance. You do not give up any legal rights by signing this form.

What other choices do I have?
You can choose not to be in the study. Instead of being in this study, you can receive treatment that is already available, such as the antiviral drugs prescribed by your doctor. You will not have access to Losartan to treat your COVID-19 symptoms if you are not in this study.

How will my privacy be protected?
The researchers will keep your identity confidential, as required by law. Your health information is protected by a federal privacy law called HIPAA. If you sign this consent form, you give permission for KUMC to use and share your health information. You can decide not to sign this form and not be part of the study.

Dr. Salathe and members of the research team will only use and share information that is needed for the study. They will collect health information from the study activities and from your medical record. Your medical records may contain information such as name, address, phone, date of birth, social security number, or other identifiers. Others at KUMC might need to look at your research records. They include KUMC Research Institute, the

Institutional Review Board or other committees and offices that review and monitor research studies.

If you sign this form, you give the study team permission to share your research information with people outside KUMC. These groups or agencies may make copies of study records for audit purposes. Some of these groups might not have to comply with the HIPAA law, but they have agreed to protect your information. These groups may include:

- Groups that process lab samples or help manage the study
- Experts who inspect the study information to see if the study is being done correctly and if it is still safe to continue
- The FDA and similar groups in foreign countries
- Other federal agencies that oversee human research (if a study audit is performed)
- Ethics committees that review the study for other locations

The information shared about you will not have your name, social security number, address, phone number or other direct identifier. It may have other identifiers such as your age, date of birth sex, and medical history. It will also be labeled with your research ID number. The KUMC study team will keep the list that matches your name to the research ID number, but they won't share it outside KUMC. By taking these steps, there is less risk that your personal identity and information will be seen by others who shouldn't have it.

Researchers plan to use your information indefinitely unless you cancel your permission. Any research information that is put in your medical record will be kept indefinitely. You have the right to see and copy any study information that is included in your medical record.

The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study.

Will I be told about research results?
You will be told about any study results that directly affect your medical care. Overall results of the study will not be given to patients, but may be used in a publication or presentation about the study in the future. If this happens, any information that may be able to identify you will be removed.

How will my research information and specimens be used in the future?
In the future, researchers at KUMC and at other locations might re-use the information and specimens from this study for other research. If that happens, information that could identify you will be removed first. You will not be asked if you agree to the future research that has identifiers removed.

Can I stop being in the study?
You may stop being in the study at any time. Stopping will not prevent you from getting treatment or services at KUMC. If you decide to withdraw from the study, or researchers determine that Losartan is not working for you, we will continue to follow your progress after you stop taking the study drug for up to 14 days, or until you have been discharged from the hospital.

You can choose to cancel your permission for researchers to use your health information. If you want to cancel your permission, please write to Dr. Salathe. The mailing address is Matthias Salathe, MD, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160. If you cancel permission to use your health information, you will be withdrawn from the study. The researchers will stop collecting any additional information about you unless they need information about a side effect of Losartan. They are permitted to use and share information that was gathered before they received your cancellation.

Could my participation be stopped early?
This study might be stopped, without your consent, by the investigator, or by the FDA. Your participation also might be stopped by the investigator if it is in no longer safe for you or if you do not follow the study requirements.

The University of Kansas Medical Center and the investigator are not obligated to provide you with any Losartan if the study is stopped early. Your physician will decide about future treatment, if it is needed.

Who can I talk to about the study?
Dr. Salathe or other members of the study team should answer all your questions before you sign this form. They will also tell you if they learn anything new that might affect your decision to stay in the study. You can talk to the researchers if you have any more questions, suggestions, concerns or complaints. If you have questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the KUMC Institutional Review Board at (913) 588-1240. You may also write the Institutional Review Board at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160.

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.

CONSENT

Dr. Salathe or the research team has given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

By signing this form, you say that you freely and voluntarily consent to participate in this research study. You have read the information and had your questions answered.

You will be given a signed copy of the consent form to keep for your records.

Option 1: You give permission to have your treatment progress/data followed and recorded by the study team for this research study, and **receive** Losartan to treat my COVID-19 symptoms.

☐YES ☐NO

Option 2: (Only provide answer if you chose No to the above request)

You give permission to have your treatment progress/data followed and recorded by the study team for this research study, but wish to **not receive** Losartan to treat my COVID-19 symptoms.

☐YES ☐NO

_____

Print Participant's Name

_____ _____ _____

Signature of Participant Time Date

_____

Print Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

CONSENT BY A SURROGATE DECISION-MAKER

You are a relative or other individual who is making decisions on behalf of a person with COVID-19. You are being asked to approve his or her participation in the research study described in this consent form.

By signing this form, you agree that Dr. Salathe or the study team have given you the information you need to make your decision. The study team has explained what will happen in the research. They explained any inconvenience, discomfort or risks that should be considered. You have had a chance to get your questions answered. At this time, you agree to have the participant enroll in the study.

If the participant becomes able to consent to research during the course of the study, the information in this form will be presented again so they can provide their own consent.

You will be given a signed copy of the consent form to keep for your records.

Option 1: You give permission to have the treatment progress/data of the participant followed and recorded by the study team for this research study, and authorize the participant to **receive** Losartan to treat their COVID-19 symptoms.

☐YES ☐NO

Option 2: (Only provide answer if you chose No to the above request)
You give permission to have the treatment progress/data of the participant followed and recorded by the study team for this research study, and authorize the participant to **not receive** Losartan to treat their COVID-19 symptoms.

☐YES ☐NO

As legal guardian or representative, I, _____,
Print Name of Guardian/Representative

authorize the participation of _____ in this research study.
Print Name of Participant

I understand that I may not authorize participation in this study if the individual has previously expressed wishes to the contrary, either orally or in writing.

I am (please initial one of the following categories):

_____ *Legal guardian or Durable Power of Attorney for Healthcare Decisions*

_____ *Adult or emancipated minor's spouse (unless legally separated)*

_____ *Adult child*

_____ *Parent*

_____ *Adult relative by blood or marriage*

_____ _____ _____
Signature of Legal Guardian/ Representative Time Date

_____
Print Name of Person Explaining Consent

_____ _____ _____
Signature of Person Explaining Consent Time Date