YALE UNIVERSITY SCHOOL OF MEDICINE

Yale-New Haven Hospital & Saint Raphael Campus
Yale New Haven Health Network- Greenwich Hospital
Yale New Haven Health Network-Bridgeport Hospital
Yale New Haven Health Network-Lawrence & Memorial Hospital

CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

Study Title: Colchicine/Statin for the Prevention of COVID-19 Complications (COLSTAT) Trial
Principal Investigator: Alexandra Lansky, MD
Funding Source: American Diabetes Association, Inc.

Invitation to Participate and Description of Project

You are being invited to participate in a research study designed to look at the safety and effectiveness of the combination of colchicine+rosuvastatin added to standard of care compared to usual standard of care in patients admitted to the hospital with coronavirus infection. The purpose of the study is to find out whether colchicine+rosuvastatin can prevent progressing to severe complications from COVID-19. You have been asked to participate because you are admitted to the hospital with coronavirus infection. A total of 466 patients will be asked to take part in this study at Yale New Haven Hospital and Yale New Haven Health System.

In order to decide whether or not you wish to be a part of this research study, you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits, and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form. If you choose to participate in the study, your colchicine+rosuvastatin treatment will last until you leave the hospital and your participation will last for a total of 60 days.

Background

Infection with coronavirus can lead to difficulty breathing and the need for admission to the hospital for oxygen treatment. Once admitted to the hospital most patients with coronavirus infection will recover, but approximately 44% will develop severe breathing difficulty that will require ventilation with oxygen, a breathing machine or ventilator, kidney or blood pressure support or death. The complications of coronavirus infection are caused by a surge in the release of ones own inflammatory cells in response to the infection. Therefore, modifying the inflammatory response may help reduce coronavirus complications. The purpose of this study is to study whether the combination of colchicine+rosuvastatin, two commonly used drugs, both with anti-inflammatory effects and long track records of use can reduce complications of coronavirus infection.

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Colchicine is an inexpensive, extensively studied and safe anti-inflammatory medication taken by mouth that has been used to treat gout for decades. Colchicine has several anti-inflammatory effects and may also prevent uptake of the virus into cells and may limit the virus' ability to enter human cells. Recently the benefits of Colchicine were demonstrated for patients with heart disease in 2 large clinical studies.

Rosuvastatin, is a Statin, which has also been extensively studied and is commonly prescribed for the treatment of high cholesterol. It also has known anti-inflammatory effects and increases ACE2 expression which may reduce severe breathing difficulties and improve survival and reduce damage of the lining of blood vessels which is thought to cause the clotting problems linked with coronavirus infection. Rosuvastatin may have direct antiviral properties by preventing the virus from binding and entering human cells.

Both drugs are FDA approved.

If your doctor determines that you may be eligible for the study, your doctor may ask if you would like to take part in the study. You will be asked to sign this consent form before being able to participate in the study.

If you agree to participate in the study, you will be randomly selected ("randomized") to one of 2 study groups for the duration of your hospitalization. Randomization is like flipping a coin (based on chance) with a 50:50 chance of being selected for one group or the other.

1. Standard treatment with the addition of Colchicine+Rosuvastatin

2. Standard treatment alone

Follow-up Procedures after Hospital Discharge

After you leave the hospital, there will be 2 phone calls at 1 and 2 months to see how you are feeling. After hospital discharge and if you have had damage to your heart from the infection, we will ask you to have a follow-up cardiac Magnetic Resonance Imaging (MRI) to study your heart. Cardiac MRI is a non-invasive test that uses a magnet and radio wave pulses to create detailed images of the heart. Some people feel nervous (claustrophobic) while in the space that houses the MRI magnet. You may be given medication to help you relax. If you have had certain medical devices implanted (metal devices, surgical "clips", a pacemaker, implantable cardiac defibrillator or insulin pump) you may not be able to have an MRI test. It is important that you inform your study doctor of any implanted medical devices or past surgical procedures.

Risks and Inconveniences

As with any medical treatment, the combination of colchicine+rosuvastatin carries known potential risks, as well as risks that may be unknown. Your study doctor will explain the risks. The following have been identified as possible complications of the study treatment:

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- Rhabdomyolysis- condition of damaged skeletal muscle that causes release of myoglobin- protein that stores oxygen in muscles- into bloodstream and can cause kidney failure in extreme cases
- Neuromuscular toxicity
- Diarrhea- loose stools
- Pharyngolaryngeal pain- pharynx is membrane behind nose and mouth; larynx is known as the "voice box" located in your throat
- Nausea
- Abdominal pain
- Vomiting
- Fatigue
- Headache
- Leukopenia- low white blood cell count
- Granulocytopenia- less than the normal number of granular leukocytes in the blood. Can result in frequent number of bacterial infections of skin and throat
- Thrombocytopenia- causes low level of platelets, the cells that help your blood clot
- Pancytopenia- condition in which the body has too few red blood cells, white blood cells, and platelets. Can lead to excess bleeding and increased risk for infections
- Myopathy- disease of the muscle in which the muscle fibers do not function properly
- Elevated CPK-CPK stands for Creatine Phosphokinase. This is a substance that is found in the human body in places like the heart muscle and skeletal muscles. The CPK blood test is used to determine if any damage has occurred to these muscles or to other locations of the body where CPK is found. The CPK blood test is often used to evaluate if a person has suffered from a heart attack
- Myalgia- muscle pain
- Liver enzymes abnormalities
- Constipation

Potential Risks/Discomforts Associated with Non-Experimental Study Procedures

Magnetic Resonance Imaging Procedure

Magnetic resonance (MR) is a technique that uses magnets and radio waves, not x-rays, to take pictures and measure chemicals of various parts of the body. The United States Food and Drug Administration (FDA) have set guidelines for magnet strength and exposure to radio waves, and the physicians performing these tests carefully observe those guidelines.

You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the procedure at any time and we will take you out of the MR scanner. On rare occasions, some people might feel dizzy, get an upset stomach,

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have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the study staff if you have them.

During the MRI scan, patient lies in a closed area inside the magnetic tube. Some patients can experience a claustrophobic sensation during the procedure. Therefore, patients with any history of claustrophobia should relay this information to the practitioner to the study staff. It is customary that the MRI staff will be nearby during MRI scan. Furthermore, there is usually a means of communication with the staff (such as a buzzer held by the patient) which can be used for contacting the practitioner performing the scan if you find that you cannot tolerate the scan.

There are some risks with an MR study for certain people. If you have a pacemaker or some metal objects inside your body, you will not be eligible to join this study because the strong magnets in the MR scanner might harm you. Another risk is a metallic object flying through the air toward the magnet and hitting you. To reduce this risk, we require that all people undergoing the MR imaging procedure remove all metal from their clothing and all metal objects from their pockets. Nothing metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet.

This MR study is for research purposes only and is not in any way a clinical examination of the heart. The scans performed in this study are not designed to find abnormalities. The primary investigator, the MR technologist, and the Magnetic Resonance Research Center are not qualified to interpret the MR scans and are not responsible for providing a diagnostic evaluation of the images. If a worrisome finding is seen on your scan, a radiologist or another physician will review the relevant images. Based on his or her recommendation (if any), the primary investigator or consulting physician will contact you, inform you of the finding, and recommend that you seek medical advice as a precautionary measure. The decision for additional examination or treatment would lie solely with you and your doctor.

Benefits

You may or may not receive direct benefit from taking part in this study. However, your taking part in this research may benefit patients with coronavirus infection in the future. If you receive treatment with the study drug, you may benefit from participating in this research by having less inflammation and better outcomes.

Economic Considerations

The medications (colchicine+rosuvastatin) and procedures (Cardiac MRI) done solely for the purposes of this study will be covered by the sponsor of the study. All other tests and procedures performed if you were not in the study will be the responsibility of you or your insurance provider to pay for. Your doctor and the study team will go over what you may be expected to pay for and what will be covered as a part of the study with you. You will not be paid or receive financial compensation to take part in the study.

Treatment Alternatives/Alternatives

The current alternative to this study is to decline to take part in the study and to undergo usual care as recommended by your doctor.

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Confidentiality

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. To safeguard the confidentiality of subjects' data, we will code data with numbers (and remove identifying information), store research materials in locked cabinets, and use computers with password-protection. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and telephone number. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study.

The information about your health that will be collected in this study includes:

- Research study records
- All information in your medical record, the results of physical exams, laboratory test results, MRI and CT scan results, medication records and other tests, your medical history and other data collected during the study
- The following study-related information:
    - Records about phone calls made as part of this research
    - Records about your study visits
    - Diaries or questionnaires

Information about you and your health which might identify you may be reviewed, used by or given to:

- The Principal Investigator*:*
- The study sponsor or the sponsor's designee who may be conducting parts of the study on behalf of the sponsor
- Health care providers who provide services to you in connection with this study
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan
- Individuals who review your medical records for billing purposes
- Co-Investigators and other members of the study team

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- Representatives of the Food and Drug Administration and the Yale Institution Review Board (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance and protection of research subjects
- Representatives of the Department of Health and Human Services (DHHS)

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale New Haven Health System are required to comply with HIPAA regulations and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

The sponsor will see the research information we collect about you when we monitor the conduct of this research study. The "Sponsor" includes any persons that work for or are hired by the sponsor to conduct research activities related to this study. For this study, the sponsor is Yale University.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies.

This authorization to use and disclose your health information collected during your taking part in this study will never expire.

In Case of Injury

If you believe that the illness or injury is a result of the research, please contact your study doctor, Alexandra Lansky, MD at 203-737-2142 as soon as possible.

If you become ill or are hurt while you are in the study, get the medical care that you need right away. You or your insurance company will be responsible for medical costs of treatment and care that occur during the study. However, if you experience an illness or injury resulting from the study drug, you and/or your insurance company will not be billed for diagnosis, care and treatment as long as the study protocol was followed by your study doctor, instructions provided to you by your study doctor were followed, and the illness or injury was not a result of a pre-existing condition or was not an expected risk from standard treatments for your condition.

For the treatment of injuries sustained as a direct result of participation in the study, the study sponsor will cover the expenses. No additional financial compensation for injury or lost wages is available.

You do not give up any of your legal rights by signing this form. If you have any questions regarding research related injury, or where to obtain care, you should contact your research study doctor Alexandra Lansky, MD at 203-737-2142.

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Voluntary Participation and Withdrawal

You are free to choose not to take part in this study. Your participation in this study is voluntary and deciding not to participate will involve no penalty or loss of benefits to which you are entitled.

Withdrawing from the Study

If you choose to participate and later change your mind, you are free to stop and withdraw from this study at any time during its course. If you choose to withdraw, data collected up until your withdrawal may still be used in the research study. All identifying information will be destroyed upon your withdrawal. To withdraw from the study, you can call a member of the study team at any time and tell them that you no longer want to take part. Your study doctor will advise you if there are any precautions to be taken should you withdraw from the study prior to completion of all study follow-ups.

Involuntary Withdrawal from the Study

The researchers may withdraw you from participating in the research if necessary. Your study doctor may end your participation if he/she determines that it is not in your best medical interest to continue taking part in the study. The sponsor of the study may decide not to continue the study resulting in early withdrawal of subjects from the study. Your study doctor will advise you of any special precautions that may need to be taken should this occur.

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor*:*

Alexandra Lansky, MD

Yale Internal Medicine/Cardiology

PO Box 208017

New Haven, CT 06520-8017

If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

New Findings

If significant new findings develop during the course of this study which may relate to your willingness to continue participating, your study doctor will provide this information to you. You may be asked to sign a revised consent form if this occurs. You do not waive any of your legal rights by signing a revised consent form.

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Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

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.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator *Dr. Alexandra Lansky at 203-737-2142*.

If you would like to talk with someone other than the researchers to discuss problems, concerns, or questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at *203-785-4866.*

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Authorization

I have read (or someone has read to me) this form and have decided to participate in the COLSTAT Trial described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form. By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form.

Printed Name of Patient: _____

Signature of Patient: _____

Date: _____ Time: _____

Printed Name of Legally Authorized Representative of Patient:

_____

Signature of Legally Authorized Representative of Patient:

_____

Date: _____ Time: _____

Printed Name of Investigator Obtaining Consent: _____

Signature of Investigator Obtaining Consent: _____

Date: _____ Time: _____

or

Printed Name of Person Obtaining Consent: _____

Signature of Person Obtaining Consent: _____

Date: _____ Time: _____

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