HealthPartners, Inc.
Consent to Participate in a Research Study

Study Title	Impact of colchicine and low-dose naltrexone on COVID-19 disease progression and clinical course in hospitalized patients
Study Investigator	Dan Delaney, PharmD Department: Pharmacy (Methodist Hospital) Daytime Phone: 952-993-7197 24-hour contact number: 651-254-9900
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Introduction

You are invited to participate in a research study. In order to participate, you must be at least 18 of age and currently hospitalized with COVID-19 (corona virus). Taking part in this research study is voluntary.

To make reading this consent form easier, please note that the word "you" refers either to you if you are the patient (research participant), or to the patient (research participant) if you are his/her family member.

Important Information about the Research Study

Things you should know:

- The purpose of the study is to find out if two different drugs, naltrexone and colchicine (taken alone or together), reduce the chance that patients with moderate COVID-19 will develop more severe symptoms when compared to the usual course of care.

  If you choose to participate, you will be asked to allow us to randomly assign you to one of four study groups: (1) one that will receive two study drugs, (colchicine + naltrexone), (2) one that will receive only colchicine, (3) one that will receive only naltrexone, (4) and one that will receive no study drugs. All patients, no matter which group, will also receive the usual care provided to patients with COVID-19. While the specific treatment patients with COVID-19 receive will depend on their symptoms, those who are hospitalized will often be given antiviral drugs and corticosteroids to help slow production of the virus and prevent an excessive immune response. Patients may also receive supplemental oxygen therapy, and medications to prevent complications of COVID-19, such as blood clots.

  If you are in any of the three groups receiving study drugs, you will be asked to take these medications until you are discharged from the hospital, but no longer than 28 days. If you are not receiving study drug, you will not be asked to do anything different during the study. Some extra labs may be collected. These include labs that are drawn to monitor the condition of patients with COVID-19, and will help us understand how your body is responding to the virus. These labs help us understand how your liver (hepatic panel), immune system (CBC with differential) and kidneys (serum creatinine) are functioning, and if there are concerns for blood

clotting problems (d-dimer) or iron deficiency (ferritin).We will also review your medical records for information about the course of your treatment until the time of your discharge from the hospital.

- Risks and discomforts from this research include those related to taking the study drugs, as well as those related to research in general. Colchicine can cause nausea, diarrhea, and vomiting. Low dose naltrexone can cause headaches, dizziness, anxiety, and insomnia. There is also the risk of the loss of the confidentiality of your health information, but the study team will take measures to prevent this from happening.
- The study may or may not benefit you directly, but this cannot be guaranteed. By being in this study, you are helping us learn more about the study drugs and whether the study drugs help to effectively treat other patients with COVID-19.
- Taking part in this research study is voluntary. You don't have to participate and you can stop at any time.
- Alternative procedures or course of treatment include:
    - Receiving the usual care provided to patients with COVID-19 as described above.

Please take time to read this form and ask questions before deciding whether to take part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you decide to take part in this study, you will be asked to sign and date this form and will be given a copy of the signed and dated consent form.

Why am I being asked to participate?

You are being asked whether you would like to participate in a research study about moderate COVID-19 because you recently tested positive for this virus and are hospitalized due to your symptoms, or you were diagnosed with COVID-19 after your admission to the hospital and your doctor believes this finding contributes to your current hospitalization.

What is the purpose of this study?

In this study, we want to find out if the drugs colchicine and naltrexone, either alone or combined, reduce the chance that patients with moderate COVID-19 will develop more severe symptoms compared to the usual care. A second goal of the study is to find out if there is a difference between the groups who receive colchicine or naltrexone alone (compared to those who get colchicine and naltrexone together) on overall patient outcomes and treatment needs.

Although colchicine and naltrexone are approved by the FDA for certain uses, they have not been approved specifically for use in patients with COVID-19. Colchicine is a medication that has been used to treat symptoms of gout, a condition that causes joint pain and swelling. Naltrexone helps people with alcohol or narcotic dependence reduce or stop their use of these drugs. Both of these medications interfere with cytokines, or proteins that are responsible for the extreme immune response seen in severe COVID-19 cases. While Colchicine restricts the production of cytokines, naltrexone limits their release. This study will investigate the use of these drugs for a new indication (use) and will help us determine if using them together is better than each alone for the treatment of COVID-19.

Where will this study take place?

This study will take place at both Regions Hospital in St. Paul, MN and Park Nicollet Methodist Hospital in St. Louis Park, MN. We expect to enroll up to 180 subjects.

What is involved if I take part?

If you agree to take part in this study, you will be asked to sign this consent form before any study-related procedures are performed. The investigator and research team will ask you questions and review your medical records to see if you qualify to be in the study.

If you meet all criteria to be in this study, you will be randomized to one of 4 groups. Randomized means being assigned to a group by chance, like flipping a coin or drawing names out of a hat. You have a 25%, or one in four, chance of being assigned to each group.

Group 1 will receive 0.6mg of colchicine orally twice a day, along with usual care. **Group 2** will receive 0.6mg of colchicine orally twice a day, 4.5mg of naltrexone once daily, and usual care. **Group 3** will receive 4.5mg of naltrexone orally once daily and usual care. **Group 4** will receive usual care and no study drugs. You cannot choose which group you will be in.

As a subject, you will be responsible for:

- telling the investigator if you are feeling bad or worse than before
- following the directions of the investigator and research team

What will happen during the study?

All study participants will be screened, enrolled, and randomized. The schedule of future events will be based on your length of stay at the hospital and study group. After randomization, some study-specific labs may be done if they are not ordered by your doctor as part of your usual care.

Time Point	**Study Events**	**How long will this take?**	**Reminders**
Screening/ Enrollment – Day 1	● Answer questions about yourself to help the study team make sure you are eligible to participate. ● Review and sign this consent form	60-90 minutes	
Randomization– Day 1	● Be randomized to a study drug group or usual care ● Receive initial dose of study drug (if assigned to one of three treatment groups)	15 minutes	
Days 2-28	● Receive study medication 1-2 times a day if in one of the treatment groups ● Study team will draw study labs (in addition to usual care) to monitor illness/assess safety	30 minutes	Will continue up to 28 days, but may stop sooner if discharged.

Are there any risks to me?

There may be side effects from the study drug. Many side effects go away, but sometimes they can be serious, long-lasting, or may never go away. There may be other side effects that we don't know about yet, so be sure to tell the investigator about any unusual symptoms.

Risks of Colchicine

Common risks of colchicine, reported in about 20% of users, affect the stomach and gastrointestinal system. These may include: diarrhea, nausea, and vomiting, but are not often seen at the low doses used for this study. If you experience these issues, the study team may reduce your dosage for this study to one 0.6mg tablet per day.

Rare side effects (<1%) include damage to the liver (hepatotoxicity), reduced ability of the bones to make immune cells (bone marrow suppression), and muscle damage (myotoxicity)

Poor kidney function is another potential risk, and this most likely to happen in patients taking certain medications. The study team will tell you if you are not eligible for this study if the medications you are taking would make it unsafe for you to do so.

Risks of Naltrexone

Common risks of naltrexone, affecting more than 10% of users, include: headaches, dizziness, nausea, insomnia, and anxiety. These side effects are typically seen at higher doses than what is being given for this study.

Naltrexone is well-tolerated at higher doses than what is used for this study, but study team members will monitor patients for rare risks like damage to the liver (hepatotoxicity).

Opioid withdrawal is another potential issue, and this most likely to happen in patients who are receiving chronic opioid therapy. The study team will tell you if you are not eligible for this study if the medications you are taking would make it unsafe for you to do so.

The risks of colchicine and naltrexone for an embryo, fetus, or nursing infant, are not well know at this time. If you are pregnant or breast feeding, you should not participate in this study. If you discover you are pregnant during the study, you must tell the investigator immediately.

Are there any benefits to me?

You may or may not benefit from being in this study. Your disease or condition could improve in the following ways: lessening of COVID-19 symptoms or shorter recovery time from your current illness.

It is also possible that your condition could stay the same or even get worse. We hope the information learned will help other patients with COVID-19 in the future.

How is this study being funded?

This research is supported by a grant from the Park Nicollet Foundation.

How much will it cost to participate?

You will not need to pay for the study drugs or any lab tests done solely for research purposes. Any procedures and tests performed while you are in the hospital that will be for your routine medical care (and not specifically for research) will be charged to you or your insurance company as they normally would.

Will I be paid to participate?

You will not be paid to participate in this study.

How long will I be in the study?

You will be in the study for the duration of your hospital stay for COVID-19. If you are randomized to a group receiving one or more study drugs, you will be asked to take medication until you are discharged, but no more than 28 days.

The study may be stopped early by the investigator. You could be asked to stop being in the study for any of the following reasons:

- for your safety
- if you do not follow our directions for this study
- if you become pregnant

Do I have to be in this study?

You do not have to be in this study. If you start the study, you may stop at any time. There is no penalty or loss of benefits if you don't want to participate, and your decision won't affect your regular medical care.

You may decide to participate now, but change your mind and withdraw from the study anytime without penalty or loss of benefits. If you decide to withdraw before the study ends, let the investigator and/or study team know. You may do so by contacting the investigator at the number on this consent form (a copy of which will be provided to you) or study coordinator and stating your intention to stop participating. Although we will no longer collect data on your hospital stay after your withdrawal, there may be special procedures to follow for your safety.

Your only choices are to participate, or not to participate. It is up to you whether you want to be in this study.

What if I am harmed from being in the study?

If you get hurt or sick from being in this study, you should let the investigator/study team know as soon as possible. If you are in the hospital at the time of your injury, your providers will ensure you receive the care that you need. The study team will not cover the cost of treatment provided to you for harm caused by your participation in this study. You will be responsible for the cost of any medical services provided to you in the study-related illness or injury. By signing this form, you are not giving up any of your legal rights.

Will my records be kept confidential?

Your study records will be kept as confidential as possible. This is further described in the HIPAA Authorization. Please know that at any time, your study records may be reviewed by the United States Food and Drug Administration (FDA), the HealthPartners IRB, or the study team.

Any information we collect on you for this study, even if identifiers are removed, will not be used or distributed for future research studies.

All tests, assessments, and procedures done as part your hospital stay (other than your use of the study drug, if applicable) will be done as part of your treatment for COVID-19 and not solely for research. If you would like to know the results of any tests performed during your hospital stay, consult with your care provider.

What if there is new information about this study?

If we learn any new information about this study that might make you change your mind about participating, we will tell you.

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.

Who oversees this study?

HealthPartners Institutional Review Board (IRB) has approved this study. The IRB is a committee of people who review all research studies at HealthPartners to check that they meet federal laws and ethical standards.

IRB approval only means it is ok for the study to begin. *Only you* can decide if being in this study is the right decision. Feel free to talk about this study with your family, friends and personal doctor before you decide.

Who do I contact?

If …	**You should contact**	**Contact information**
You are harmed by the research or have questions about clinical procedures in the study	Dan Delaney, PharmD (24 Hour Phone Line)	651-254-9900
You have questions about your rights as a research subject	IRB office	952-967-5025

Information about Confidentiality and HIPAA Authorization

The Privacy Rule of the federal Health Insurance Portability & Accountability Act (HIPAA) is a law that protects the confidentiality of your personal health information. This Authorization describes your rights and explains how your health information will be used and disclosed.

Why is access to my health information being requested?

To help answer the research questions, the investigator and research team will use and store personal health information about you. We are asking your permission to use and share it with others, as explained below. If you don't give this permission, you won't be able to take part in the research study.

What information will be collected and used?

When you are a subject, we will collect health information about you that also includes your name, address, telephone number, or other data that could identify the health information as yours. Under HIPAA, this health information is protected and can't be used without your permission, unless otherwise permitted by law. If you sign this authorization, you are giving permission for HealthPartners to use and disclose your personal health information as described below.

The following are examples of personal health information that may be collected for this study:

- results of tests and procedures
- information about your medical conditions and history

The collected information may contain your name, address, telephone number, social security number, health plan number, date of birth, medical record numbers, dates relating to various medical procedures, and/or other identifying information.

Who will see my protected health information?

By signing this Authorization, you allow the research team to use your personal health information to carry out and evaluate this study. You also allow access to your personal health information (including direct access to your medical records at HealthPartners/or Dental Clinic) to the following:

Who may have access:	**Purpose:**
HealthPartners consultants and employees, including IRB members	To protect the rights and safety of subjects and make sure the study information is correct
Organizations that regulate research (such as the FDA, Office for Human Research Protections (OHRP), or similar government agencies in the US and other countries)	To make sure applicable laws are being followed
Organizations that grant accreditation to hospitals and research programs	For HealthPartners to remain accredited

Will you keep my health information confidential?

We will keep your personal health information as confidential as possible. We will only share it as described above or if required or permitted by law. It is not likely your information will be given to others without your permission. However, once your information leaves HealthPartners, we can't control how it is used, and it will no longer be covered by the HIPAA Privacy Rule.

Will other people know that I was in this study?

If the results of this study are published, your name or other personal information will not be included.

How long will my personal health information be used?

Access to your personal health information begins as soon as you sign this form. This authorization expires when the study is finished, data analysis is complete, and the study records have been destroyed.

What if I change my mind?

If you don't want us to use and disclose your personal health information anymore, you must let the investigator know in writing. If you need help with this, you can ask the research team or call the HealthPartners IRB office at 952-967-5025.

If you withdraw permission for us to use your personal health information:

- you can't continue in the research study
- we will stop collecting health information from you
- we will still use and disclose any information that we gathered while you were a subject
- there will not be any penalty or loss of benefits to which you are otherwise entitled

Can I see my study records?

You can see your study records at any time.

Subject name: _____

- I have read this form and the research study has been explained to me.
- I have been given the chance to ask questions, and my questions have been answered. I have been told who to call if I have more questions.
- I agree to be in the research study described above.
- I will receive a copy of this consent form after I sign it. A copy will be put in my medical record and/or study record.
- I am not giving up any of my legal rights by signing this form.

_____

Subject signature Date

_____

Witness signature (if applicable*) Date

**Use when the subject or legally authorized representative cannot read the consent (for example, subject is blind, illiterate, or does not speak English). The witness must be present for the entire consent discussion. The witness signature means that the information in this document was presented to the subject, and the subject appeared to understand it.*

_____

Representative signature Date

Relationship to Subject:_____

For Site Use only:

- I have carefully explained to the subject the nature and purpose of this study.
- The subject has been given enough time and an adequate place to read and review this form.
- The subject has had a chance to ask questions and receive answers about this study.
- I have explained and discussed the nature of the research
- I have explained and discussed potential risks and benefits
- The alternate treatments available to the subject and the benefits and risks of each

Name of person obtaining informed consent (print) Title Phone number

Signature of person obtaining informed consent Date