

Protocol Title:

**Efficacy of Novel Agents for Treatment of
SARS-CoV- 2 Infection Among High-Risk
Outpatient Adults: An Adaptive
Randomized Platform Trial**

NCT Number:

NCT04354428

Document Date:

17 August 2020

INFORMED CONSENT FORM

TITLE: Efficacy of Novel Agents for Treatment of SARS-CoV-2 Infection Among High-Risk Outpatient Adults: An Adaptive Randomized Platform Trial

LOPINAVIR/RITONAVIR ARM

PROTOCOL NO.: UW-ICRC Protocol #55
WIRB® Protocol #20200801

SPONSOR: University of Washington

INVESTIGATOR: Name
Address
City, State Zip
Country

**STUDY-RELATED
PHONE NUMBER(S):** Phone Number
Phone Number (24 hours)
[24 hour number is required]

We are asking you to be in a research study. This study is being conducted by [Site Name] and the University of Washington Virology Research Clinic, which is based in Seattle, Washington. This form describes the study procedures and gives you information to decide whether you wish to be in the study. Being in the study is entirely your choice (voluntary).

What should I do?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. Take time to consider this, and talk about it with your family and friends.

The first part of this consent form gives you a **summary of this study**.

The second part of this consent form gives you more details about the study procedures and any risks to you.

PURPOSE OF THE STUDY

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus that causes coronavirus disease (COVID-19). The purpose of this study is to understand if taking lopinavir/ritonavir (LPV/r) may be used to help treat people infected with early SARS-CoV-2 infection. Currently, there are no FDA-approved treatment drugs for SARS-CoV-2 infection or COVID-19.

LPV/r is an investigational antiviral medication that has been used to control HIV infection. The FDA first approved the LPV/r in 2000 and safety and tolerability are well described. It is currently not known if LPV/r is an effective treatment for COVID-19.

This study will show us whether early treatment of SARS-CoV-2 infection is effective at preventing more severe illness. We will study these medications in people who are well enough to be treated in their homes. We will study the medication in people who are at increased risk for developing complications of SARS-CoV-2 infection, and also people who do not have identified risk factors for more severe infection.

If you choose to be in the study, you will be assigned by chance (chance is like flipping a coin) to either LPV/r or vitamin C. You will take a double dose of LPV/r or vitamin C by mouth twice daily for one day, followed by a single dose by mouth twice daily for 9 days, for a total of 10 days of treatment.

Pregnant and lactating persons will be eligible for enrollment into this study. LPV/r has been shown to be safe in pregnant women. Participants taking hormonal contraceptives to prevent pregnancy will be educated that they will need to use a backup form of birth control during the study period.

STUDY PROCEDURES

We are testing LPV/r in adults who have had a laboratory confirmed SARS-CoV-2 infection within the past 72 hours and have symptoms of COVID-19. We are inviting you to participate because you have been referred by your healthcare provider or have been self-referred. Here is what the study involves:

- You will be contacted by our research team and asked to join this study. You will be in this study for approximately 28 days and no in-person visits are necessary – every interaction will occur via telephone, telehealth, internet, or mail. If you are selected for a substudy you will complete extra sample collections throughout the study and 28 days after your first visit.
- We will ask you to complete a brief enrollment survey about medical history, current & past symptoms, date of COVID-19 diagnosis, current use of medicines, and demographics. These questions will be asked either by telephone or answering questions in an online survey.
- We will ask you to sign Health Insurance Portability and Accountability Act (HIPAA) forms so we may access your COVID-19 related medical records.
- You will complete a short survey about your current health for 14 days. We will ask you to meet with study staff via telehealth roughly every 3-4 days during the study. You will have the option to request to meet with study staff via telehealth more frequently. We will ask you to check your temperature, oxygen saturation, pulse, and respiratory rate twice a day. We may also ask you to check your heart rhythm using a device. We will provide all supplies to you to do these assessments. The procedures will take about 30 minutes each day.
- You will be asked to self-test for your current COVID-19 status by swabbing the inside of your nose with a special swab called a nasal swab. We will ask you to repeat this procedure with a new swab daily while in the study. Once you have swabbed the inside of your nose, you will put your swab in a special tube for storage.
- You may also be asked to prick your finger to collect drops of blood called dried blood spots on a special card. We may ask you to collect these blood spots at enrollment, partway through the study, and at the end of the study.
- We will provide you with all the supplies you need to collect your samples. The supplies will arrive in a couriered package, and we will give you envelopes and postage to either mail them back or a courier will come collect them.
- To test for novel coronavirus, the swabs will be sent to the University of Washington. Your results may not be available for weeks after the study is completed. When your results are available, we will provide them to you. These swabs are not part of routine clinical care.

This study does not replace or affect any care you might receive from your doctor.

RISKS, STRESS, OR DISCOMFORT

Because there are always some risks to taking part in a research study, we have listed some of the most likely risks of participation in this study here:

Possible Risks related to LPV/r treatment

- Nausea
- Occasional dizziness
- Diarrhea
- Abdominal pain

There are also rare but serious risks of LPV/r treatment, like:

- Serious allergic reaction
- Liver problems
- Pancreatitis
- Heart rhythm problems
- Life-threatening drug interactions

We may provide you medications to provide symptomatic relief from diarrhea (loperamide) or nausea (ondansetron) related to study medication.

Possible Risks related to Nasal Swabs or Fingerprick:

- Swabbing your nose may cause mild discomfort, watery eyes, or sneezing.
- Drawing a few drops of blood from your finger for the dry blood test may cause temporary discomfort from the needle stick, bruising, and infection.

Some questions we might ask you are sensitive and may make you feel uncomfortable. You do not have to answer any question you do not want to. There is a risk that your privacy could be breached. We will do everything we can to make sure that this does not happen.

BENEFITS OF THE STUDY

Possible Benefits:

If you are in the group that receives LPV/r, and if it proves to reduce your chances of developing severe COVID-19 disease or shortens the duration of your disease.

If you are in the group that receives vitamin C, this may help to support your immune system but you will not receive study drugs.

You may benefit from participating in the study, but this cannot be guaranteed.

Your Other Options:

There are currently no approved drugs to treat COVID-19. However, your clinician may choose to prescribe you drugs including LPV/r to treat COVID-19 if they think the drugs may help, even though no drugs yet are known to help or FDA-approved. You do not have to participate in this study.

Your other choices may include:

- Taking part in another study.
- Working with your doctor to manage your COVID-19 outside of a study.

You may want to talk to your doctor about your choices before agreeing to participate in this study.

SOURCE OF FUNDING

The [Site Name] and/or the University of Washington is receiving financial support from the Bill & Melinda Gates Foundation.

DETAILED STUDY INFORMATION

The following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will offer you a copy of this form to keep for future reference.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor. If you decline to participate your doctor will still give you care for your COVID-19 diagnosis.

Why am I being asked to participate?

You are being asked to take part in this study because you are an adult who has had a laboratory confirmed SARS-CoV-2 infection result within the past 72 hours with symptoms of COVID-19 disease.

Why is this study being done?

The purpose of this study is to understand if the medication used to treat HIV infection called LPV/r can reduce the length and/or severity of COVID-19 disease. The study will also look at whether the drugs are safe for patients with COVID-19. While LPV/r are approved by the Food and Drug Administration (FDA), using the drugs to treat COVID-19 is investigational and is not approved by the FDA.

The manufacturer of the drugs that are being used in this study are not involved with the conduct of this study. AbbeVie, the maker of LPV/r, has donated the medication for this study. The study will provide the assigned drug at no cost to the research participant.

How many people will take part in this study?

About 346 people will take part in this study.

What will happen if I take part in this research study?

If you are eligible to be in the study and you choose to take part, then you will need the following tests and procedures:

- You will be asked to complete surveys by telephone, web, or video chat.
 - You will be asked to attend telehealth visits with the study staff.
 - You will be asked a series of questions about your health, including your current COVID-19 symptoms, including shortness of breath, fever, and cough.
 - You will be asked if you have any symptoms that can be associated with taking LPV/r.
 - You will also be asked other questions about your medical history, current vitals, current & past symptoms, date of COVID-19 diagnosis, current use of medicines, and demographics.

- You will self-test to monitor your COVID-19 nasal shedding. This will be done by swabbing the inside of your nose.
- You may be asked to collect a few drops of blood by pricking your finger and collecting it on a piece of filter paper we provide you. This blood will be used to test for the level of drug or COVID-19 antibodies in your blood, infection fighting cells, or inflammatory markers. If other tests directly related to COVID-19 are developed, we may use the blood to understand your immune response using those tests.
- We will ask you to check your temperature, oxygen saturation, pulse, and respiratory rate twice a day. We may also ask you to check your heart rhythm using a device. We will provide all supplies to you to do these assessments and will teach you how to use them. The procedures will take about 30 minutes each day.
- You will receive an email daily with a link to a survey to document when you take the treatment (LPV/r or vitamin C). The survey will ask how you are feeling, and if you have collected a nasal swab. We would like you to complete this once a day for the 14 days you are enrolled in the study, and on Day 21 and Day 28.
- You will be asked to complete a final brief survey by telephone or internet at completion of the study. Some of these questions may include how you are feeling, if you thought you were taking LPV/r or vitamin C, and your thoughts on participating in the study.

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance, like flipping a coin. A computer program will place you in one of the groups. You will have an equal or 50% chance (one in two) of being placed in the LPV/r treatment group vs. the vitamin group. You and your doctor will not know which group you are assigned to. The study pharmacist will know your group assignment & will disclose the information at the end of the study, or if there is a medical emergency and it is required to do so.

You will be provided with a supply of pills. You will take a double dose by mouth twice daily for one day. Then, you will take a single dose by mouth twice daily for the next 9 days, for a total of 10 days of treatment. You will be provided with dosing directions when you receive the medications.

- **If you are assigned to the group receiving LPV/r**, you will be taking 800 mg-200 mg LPV/r twice daily on day one, and then 400 mg-100 mg of LPV/r twice daily for the next 9 days.
- **If you are assigned to the group receiving the vitamin C pill**, you will be taking 1,000 mg of vitamin C twice daily on day one, and then 500 mg of vitamin C twice daily for the next 9 days.

Timing of study visits and procedures:

- The initial enrollment survey will take approximately 15 minutes.
- The initial enrollment visit with the study staff will take approximately 45 minutes, to up to 2 hours.
- The follow up visit (days 2, 4 and 9, and 14) with the study staff will take approximately 20 minutes.
- The daily follow up survey (days 2-14) will take you approximately 15 minutes.
- The follow-up survey at day 21 and 28 will take approximately 10 minutes.
- If you are in the sub study, you will be asked to collect a dried blood spot on day 1 and day 28, and on other days as study staff requests. You will not be asked to collect a dried blood spot more than 5 times during the study. Each collection will take approximately 10 minutes.

Study location: All study procedures will be at your own home.

Nasal swabs for SARS-CoV-2, the virus that causes COVID-19: The study will ask you to swab the inside of your nose every day from day 1 until day 14, and then collect a swab on day 21 and day 28. The study staff will teach you how to do this. Swabbing will take approximately 5 minutes.

Results of testing done for research only will not be available to you or your providers, just to the researchers in the study. You will be able to contact the study to find out your results, if you wish. We will report your test results to your local health department if required to do so by law.

Dried blood spot: If you are in the sub study, a self-test dry blood spot test sample will be drawn by pricking one of your fingers with a lancet. You will be asked to collect your blood on day 1 and day 28, and on other days as your doctor requests. You will not be asked to collect a dried blood spot more than 5 times during the study.

How long will I be in the study? Everyone will be in the study for 28 days.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study team if you are thinking about stopping or if you decide to stop. They will tell you how to stop your participation safely.

If you are admitted to the hospital, you should discontinue your study-provided medication. You may stop collecting nasal swabs and doing the daily survey. We will keep in touch with you during your hospitalization, and will request a survey 3 days after hospital discharge.

It is important to tell the study team if you are thinking about stopping so any risks from LPV/r can be evaluated, and the study team can discuss what follow-up care and testing could be most helpful for you.

The study team may stop you from taking part in this study at any time if we believe it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from the treatment?

Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Many side effects go away soon after you stop taking the LPV/r. In some rare cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side-effects you experience while taking part in the study.

For participants assigned to the LPV/r treatment group, risks and side effects include:

Likely

- Nausea
- Occasional dizziness
- Diarrhea
- Abdominal pain

Less likely

- Serious allergic reaction
- Liver problems

Rare but serious

- Pancreatitis
- Heart rhythm problems
- Life-threatening drug interactions

We may provide you medications to provide symptomatic relief from diarrhea (loperamide) or nausea (ondansetron) related to study medication.

Randomization risks: You will be assigned to receive LPV/r or vitamin C, and the group to which you are assigned may prove to be less effective or to have more side effects than the other study treatment or other available treatments.

Dry Blood Spot: Drawing a dry blood test may cause temporary discomfort from the needle stick, bruising, and rarely, infection.

Privacy and confidentiality risks: We will make every effort to protect your confidentiality during the study. However, it is possible that others may learn that you are part of this study and they may know you have COVID-19. The most common risks we know about are family or friends worrying, getting upset or angry, or knowing that you are infected and treating you unfairly as a result.

You should feel free to discuss participation in this study with friends and family.

We will report your test results to local health departments when legally required to do so.

Although every reasonable effort has been taken, confidentiality during online communication procedures cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be viewed by others not associated with this study for unauthorized purposes.

You will be required to use your email address to gain access to the heart rhythm monitoring site.

Unknown Risks: Although LPV/r is well studied and widely used, LPV/r for COVID-19 treatment may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study team.

Are there benefits to taking part in the study?

If you are in the group that receives one of the treatments (LPV/r) and if it proves to reduce the severity of duration of COVID-19 without causing side effects that you cannot tolerate, you may benefit from participating in the study, but this cannot be guaranteed.

If you are in the group that does not receive LPV/r, you may have the same or fewer side effects associated with the other groups, but this cannot be guaranteed.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Taking part in another study.
- Working with your health care provider to manage your COVID-19 outside of a study.

How will my specimens and information be used?

Researchers will use your specimens and information to conduct this study. Once the study is done using your specimens and information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are.

Research results: There may be times when researchers using your information or specimens may learn new information. The researchers may or may not share these results with you, depending on a number of factors.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. The results of tests may become part of your study record and may be communicated to the local health department if required. All other information collected as part of this study will be part of your study record only and will not include your name or other identifying information. All study records will be stored in a locked location or under password protection on study computers.

Only study staff will have access to your study record. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Your personal information may be given out if required by law.

Your study records may be viewed by the study team and representatives of:

- International Clinical Research Center
- The University of Washington
- Office for Human Research Protections
- The Institutional Review Board (IRB)
- The U.S. Food and Drug Administration
- [Site Name]

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.

Are there any costs to me for taking part in this study?

There are no costs to you. Any procedures done only for research will not be charged to you or your insurer.

The study will provide the drug of your assigned treatment group to you at no cost.

Will I be paid for taking part in this study?

If you complete all parts of the study, you will be paid \$400. You will receive \$300 on day 14 if you completed the surveys, nasal swabs. You will receive \$100 on day 28 if you complete the additional nasal swabs and blood spot.

What happens if I am injured because I took part in this study?

If you think you have a medical problem or illness related to this research, contact [Name] right away. They will treat you or refer you for treatment. It is important that you tell study doctors if you feel that you have been injured because of taking part in this study. Study doctors at each site are:

[Name]

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study, or if you feel you have experienced a research-related injury; see contact information above. If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers, or if you wish to voice any problems, questions, complaints or concerns you may have about the study, please contact the Institutional Review Board (IRB) at 800-562-4789, Help@wirb.com.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you or

loss benefits to which you are otherwise entitled. You will not lose any of your regular benefits. Leaving the study will not affect your medical care.

During the study, we will tell you about any new information or changes in the study that may affect your health or willingness to continue in the study.

In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, I can call the IRB® at 800-562-4789. I give permission to the researchers to use my medical records as described in this consent form.

Printed name of subject	Signature of subject	Date
-------------------------	----------------------	------

Printed name of person obtaining consent	Signature of person obtaining consent	Date
--	---------------------------------------	------

Copies to: Researcher
 Subject

Optional Consent

Future Studies

Because future studies that you may be eligible for may become available, we are asking now if you would like to learn about these studies. You can still be a part of the main study even if you say "no" to this.

I agree that I may be contacted in the future to see if I am interested in participating in further research.

☐ Yes ☐ No

Signature of subject	Date
----------------------	------

****For Sites in California****

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?

The study doctor and the study staff. [They may also share the research information with [enter SMO company name], an agent for the study doctor. delete if the site does not have an SMO]

Who might get this information?

The sponsor of this research. “Sponsor” means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information may be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Institutional Review Board (IRB)

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

May I review or copy my information?

Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?

This permission will be good until December 31, 2060.

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. 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.

Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission.

Authorization:

I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

AUTHORIZATION SIGNATURE:

Signature of Subject

Date