Informed Consent Form

A Multicenter, Adaptive, Randomized, Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients With COVID-19 (Trial H1: LY3819253 (LY-CoV555))

27 July 2020

NCT05780268

Informed Consent Form
and Authorization to Use and Disclose Protected Health Information

Sponsor / Study Title:	**University of Minnesota / INSIGHT / "A Multicenter, Adaptive, Randomized, Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients with COVID-19"**
Protocol Number:	**INSIGHT 014/ ACTIV 3**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. When the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing and dating this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent will be obtained from the subject and the subject offered the ability to leave the study if desired.

Key information:

We are asking you to join a research study about COVID-19. It is your choice whether or not you want to join. This form gives you information about the study that will help you make your choice. You can discuss this information with your regular doctor or family or anyone else you would like before you make your choice. Your choice will not affect the care you are getting for COVID-19.

What is the research question we are trying to answer?

We are studying an experimental drug called "LY3819253," made by Eli Lilly, Inc. Experimental means that the study drug is not approved by the United States Food and Drug Administration (FDA) or any other regulatory body in the world, and its use is strictly limited to research. We are trying to find out if giving this experimental drug can help people in the hospital with COVID-19 have fewer bad effects from the disease, and if it may possibly help them get better and go home faster. We are also trying to see if it is safe.

This experimental drug will provide antibodies that we think may work to fight the COVID-19 virus. We think this may possibly help, and we think this will be safe, but we are not sure and so we are doing this study.

We are asking you to join the study because you are in the hospital with COVID-19.

What do you have to do if you decide to be in the study?

The study staff at your hospital will check to see if there is any reason you should not be in the study. They will check your medical history. They will look at tests commonly done for your condition.

If you agree to be in the study, we will assign you to one of two study groups. This will be done by random chance - like flipping a coin. You will have an equal chance (50/50) of getting either the experimental drug (LY3819253), or an inactive salt solution, commonly called a placebo. Your study doctor will not decide, and will not know which of these two choices you will get. No one on the study staff will know whether you are getting the experimental drug or the inactive placebo. In case of an emergency, however, the study doctor can get this information.

You will get the study drug (either the experimental study drug or the placebo) only once, on the day you join the study (study "Day 0"). You will get it by an intravenous (IV) drip through a tube attached to a needle in your arm. This is called an infusion. The study drug is 200 milliliters, or about one cup of liquid. The infusion will take about an hour. It may sometimes take longer depending on how your body reacts to the infusion.

LY3819253 is the only thing you will be given that is completely experimental.

As part of the study you will also get a study drug called remdesivir once a day intravenously for up to 10 days while you are in the hospital, as care for your COVID-19, unless your study doctor thinks remdesivir would not be safe for you to take. Remdesivir was shown in an earlier study to help people recover more quickly from COVID-19. Remdesivir has an "emergency use authorization" in the US and many other countries. This means that the regulatory authorities are allowing its use while the company that makes it is applying for FDA approval, because there are so few drugs available to treat COVID-19.

Any other medications or treatments you will be given will be what you would usually receive in this hospital for your condition. There may be some additional procedures or testing done for study purposes. We will describe these below.

You will be in the study for 90 days. We will check on your health every day while you are in the hospital, and regularly after you leave the hospital.

If you leave the hospital after just a few days, we will ask you to either come back, or else to possibly be visited by our study staff at your home to draw a blood sample on day 3 and day 5 of the study. We will also need to take a blood sample from you on day 28 and day 90.

To be in the study, you will need to agree not to participate in any other COVID-19 study for the first 5 days you are in this study.

To be in the study, you will also need to agree to make sure that you or your partner don't become pregnant for the entire 90 days you are in the study. This is because we do not know the effects of the study drug on an unborn child. These could be serious.

The birth control requirements are described below:

Women

It is important that women who take part in this study do not become pregnant during the study. If you are a woman who can get pregnant, you must agree to either not have sex with men, or to use 2 forms of contraception. At least one form must be highly effective (less than 1% failure rate, listed below). You must agree to this for the entire 90 days you are in the study.

If you get pregnant while you are in the study, the study staff will collect information about the pregnancy, its outcome, and the health of the child after birth.

Men

If you are a man, you must agree to either not have sex with a woman who could get pregnant or to use condoms as well as a highly effective method of contraception (less than 1% failure rate, listed below). You must agree to this for the entire 90 days you are in the study.

Men with pregnant partners should use condoms for the entire 90 days you are in the study. Men should not donate sperm for the entire 90 days you are in the study.

If your partner becomes pregnant while you are in the study, the study doctor will ask your partner to sign and date a separate consent to allow the study staff to collect information about the pregnancy, its outcome, and the health of the child after birth.

Acceptable Methods of Contraception

Highly effective methods of contraception (less than 1% failure rate) include:

- Combination oral contraceptives
- Implanted contraceptives
- Intrauterine devices (IUD)

Effective methods of contraception include diaphragms with spermicide or cervical sponges.

Men and their partners may choose to use a double–barrier method of contraception that must include use of a spermicide.

If you become pregnant during the study, please let your study team know as soon as possible. We will ask to follow you until your pregnancy is over, to see if there were any problems that may have been caused by any of the study treatments.

If your partner becomes pregnant, please let your study team know as soon as possible. We will ask if we can get information about the pregnancy. If you and your partner are willing, we will ask for consent from your partner to obtain this information.

We will need to do the following things with you, and gather detailed information at these times:

Up to 1 day before you get study drug	**Day 0 (the day you get study drug)**	**Day 1, Day 3, Day 5**	**Day 2, Day 4 Day 6, Day 7, Day 14, Day 42, Day 60, Day 75**	**Day 28 and Day 90**
• Informed consent (this document) • Check to see how you are feeling • Your medical history • Contact information like telephone numbers and addresses for you and at least two close relatives or friends	• Infusion of study drug [the experimental drug or placebo] • Check whether you are taking certain medicines • Blood tests to check your health (9 mL, about ½ tablespoon) • Blood for future research (18 mL, about 1 tablespoon) • A swab of your nose for virus detection	• Check how you are feeling • Blood for future research (18 mL, about a tablespoon) • On Day 5, also check whether you have taken certain medicines, and blood tests to check your health (9 mL, about ½ tablespoon)	• Check how you are feeling These “visits” may take place by phone.	• Check how you are feeling • Blood for future research (18 mL, about a tablespoon) • On Day 28, also check whether you have taken certain medicines

Day 90 is the last day you will be in the study. If you are not completely well on day 90 we may ask to follow up with you after day 90 to see if you have gotten better.

We may need to get some information from your medical record:

- By signing and dating this consent, you agree to let us get information for this study from your medical record.
- By signing and dating this consent, you are giving us permission to contact other hospitals or medical facilities if you are admitted there during the time you are in the study. We will contact them to be sure we know how you are doing.
- We will ask you to give us information about other people we can contact if we are not able to reach you after you leave the hospital, so we can find out how you are doing.
- We will send the information we collect to the University of Minnesota (UMN) in the US where it will be stored and analyzed. In this information, only a code number, your year of birth, and a 3-letter code, that the study staff chooses, identifies you.

The study staff here at this study site is responsible for keeping your identifying information safe from anyone who should not see it.

We will send the blood and nose swab samples to a laboratory in the US for storage. We will keep them for as long as we have the funding and space to do so, which we expect to be many years. There is more information below about how we will use these samples.

Why would you want to be in the study?

If you get the experimental drug, it is possible it may help you get better, or that you may get home faster, but we do not know that.

It is important to remember that half of the people in this study will get inactive placebo, and will not get the experimental drug.

By being in this study, you will help doctors learn more about how to treat COVID-19 in people in the hospital. Because so many people are getting hospitalized with COVID-19, this could help others. There may be a large health impact if a treatment proves to be safe and is shown to be effective.

Why would you not want to be in the study?

Since only half of the people in this study will get the experimental drug, you may not receive it. Even if you do get the experimental drug, it may not be useful, or it may have harmful side effects, so being in the study would not be of any direct help to you.

What are the risks or side effects of the study treatments?

All treatments have risks and may cause side effects. These may happen to you from the study treatment.

You may have an allergic reaction, including hives, trouble breathing, or other allergic responses. Allergic reactions like these are likely to be rare, but may be severe or life-threatening.

You will be monitored very closely while you are being given the infusion of the study drug, and for at least 2 hours after the infusion is finished. We will give you prompt medical care if needed to treat any side effects from the infusion.

LY3819253 is a type of study drug called a monoclonal antibody (mAb). This general type of study drug has been approved to treat many other diseases, but LY3819253 is very early in development and has only been tested in a few subjects at the dose being used in this study. It is not yet approved for any medical treatment, or to treat COVID-19. The most common side effects of mAb's like LY3819253 are like having an allergic reaction, which may be serious:

- Chills
- Itching, rash or hives
- Swelling of the face or other parts of the body
- Low blood pressure, which may make you dizzy or cause you to faint
- A fast heart rate
- Tightness in your throat or trouble breathing
- Diarrhea (loose stools)

Getting LY3819253 may cause your body to release chemicals called cytokines. This may cause any of the reactions listed above, as well as:

- Fever
- Muscle aches
- Nausea
- Vomiting, and/or
- Headache

You will be monitored closely while you are getting LY3819253 and for a time afterwards. The rate of the infusion will be controlled to make it less likely that you would have one of these reactions. Medical personnel, equipment, and medication will be available to manage these reactions appropriately if they occur.

As of 03 July 2020, LY3819253 has been given to 18 subjects in a 'first-in-human' study for COVID-19 patients.

- 6 people received a single dose of 700 milligrams
- 6 people received a single dose of 2800 milligrams
- 6 people received a single dose of 7000 milligrams
- 6 people received inactive placebo

LY3819253 or placebo has also been given to 26 subjects in another study that is still going on.

Risks and Discomforts Associated with LY3819253

Side effects:

As of 03 July 2020, there have been no serious unwanted effects reported in subjects taking LY3819253 that were thought to be due to the study drug.

- Three subjects had difficulty breathing that was severe because of COVID-19 and not related to LY3819253; all of these subjects have either recovered or are getting better.
- One subject had chills that were mild and started a few hours after LY3819253 injection that lasted 1 hour and were thought to be related to LY3819253.
- One subject had a headache that was mild and was thought to be related to LY3819253.
- One subject had a fever that was mild and was thought to be related to LY3819253.
- Six subjects had changes in some types of white blood cell counts (above or below the normal range). This was present a few days after LY3819253 or placebo administration.
- Two subjects had a drop in the part of red blood cells that carries oxygen in the body (hemoglobin). This may cause difficulty breathing or fatigue.
- Two subjects had moderate allergic-type reactions to LY3819253 that began 30 minutes after LY3819253 infusion was started. Both reactions went away after the infusion was paused, and Benadryl was given. The infusions were completed without reoccurrence of the reaction.

Administration of LY3819253 may also cause the following risks and discomforts:

- Development of antibodies against LY3819253. This may cause your body to get rid of LY3819253 more quickly or change the effect of LY3819253 on the body. Your blood will be tested to find out whether your body made antibodies against LY3819253. We expect the risk of this to be low.
- Mixture of antibodies and other molecules in the body may occur and may cause potentially harmful deposits in tissues such as blood vessels and kidneys.
- Making your COVID-19 worse, which may be life threatening.

The fluid needed to give the study drug or the placebo may overload your body if you have problems managing fluids due to COVID-19 or other conditions. We expect this to be rare.

There are discomforts and risks associated with blood draws and obtaining a swab of your nose. These risks may include pain or bruising at the site where the blood is drawn or IV/catheter is inserted. You may feel faint. An infection at the site of the blood draw or IV/catheter insertion is possible. With the swab of your nose, you may experience discomfort, eyes watering, sneezing, or bleeding.

You will have these things done while you are in the hospital even if you are not in the study. These discomforts and risks are no different from what you would experience if they were performed as part of your regular hospital care for COVID-19.

What if you are pregnant or breastfeeding?

If you are pregnant or breastfeeding, you can still join this study. However, we do not have any information about how the study drug may affect your baby. The risks to an unborn baby or a pregnant woman may possibly be serious. Please take this into account as you make your decision about whether to join this study.

Additional information:

Here is some additional information about the study that may help you make your choice about whether you want to be in the study.

The National Institutes of Health (NIH), an agency of the US Federal government, is paying for this study.

We are required to comply with all rules and regulations for human research as well as the laws of each country where the study is taking place.

This study is taking place in several countries. We expect to enroll about 1,012 subjects around the world.

You do not have to join this research study if you do not want to. If you choose to join the study, you can stop at any time. If you choose not to join or to stop, the medical care you are getting now will not change.

If we get any new information that might change whether you want to join or stay in the study, we will tell you right away.

If you do not want to be in this study, you will still get the usual care to treat COVID-19. However, you cannot get the study treatment, because it is experimental.

What are the risks and benefits of taking remdesivir?

Remdesivir has been shown to help people who are in the hospital and moderately to severely sick with COVID-19 to get better about 4 days faster than subjects who got a placebo. You may be given remdesivir to treat your COVID-19 even if you do not join this study.

The most common side effects of remdesivir include:

- Abnormal liver function test results
- Abnormal blood clotting test results
- Constipation
- Nausea
- Vomiting
- Decreased appetite
- Headache

The abnormal liver function tests lasted longer than a few days but came back to normal levels during the study.

Some people may have some side effects after the infusion of remdesivir. Other people may have no side effects. People can have allergic reactions to drugs, including hives, trouble breathing, or other allergic responses. Allergic reactions may be severe or life-threatening. This is very rare but is also a possible effect of any drug. You will be monitored closely during the infusions, and short-term medical care will be provided to treat any side effects.

What are the costs to you?

We will give you the study treatment at no cost. We will pay for all clinic visits, lab work, and other tests that are part of this study.

You, your insurance company, or some other third-party payer must pay for all other medicines and hospital costs.

Will you be paid to be in the study?

«Compensation»

We will not compensate you for your time and inconvenience participating in the study.

What if you are hurt as part of this study?

If you are hurt because of being in this study, the study site will treat your injury right away. You or your insurance will have to pay for this treatment. The study cannot pay you or pay for any care for study-related injuries or for your illness.

A Declaration under the Public Readiness and Emergency Preparedness (PREP) Act was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a subject participating in clinical studies utilizing COVID-19 countermeasures. Because this study is covered by the Prep Act Declaration, covered persons, such as the manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States).

If you believe that you may have been harmed as a result of this research study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program. This is a program set up by the United States Government.

Information about this program can be found at https://www.hrsa.gov/cicp/about/index.html or by calling 1-855-266-2427. If you are eligible for this program, you must file a claim within one year of the administration or use of the covered countermeasure.

What happens to the blood and swab samples?

We will send the blood and swab samples to a central laboratory in the United States. You and your study doctor will **not** get the results of any tests done on these samples. We will not test your DNA (your genes). We will not sell your samples and they will not be used for research aimed at making money (commercial research). The laboratory where the samples are stored will not have any information that could identify you.

The blood samples will measure how many COVID-19 antibodies are in your blood. This will tell us how your immune system responded to your COVID-19. The swab sample will be used to determine the level of virus in your body.

Any blood or swab samples that are left over after these tests will be stored at the central laboratory for as long as we are able to keep them. We hope to use these in the future to answer other questions about COVID-19, the virus that causes it, and how people respond to treatment. You and your study doctor will **not** get any results from these tests. Some of the blood will also be given to the company that made the study drug to help them learn more about its effects.

You can withdraw your consent for us to keep these specimens at any time. Let your study team know if you do not want the study to keep your specimens anymore, and every effort will be made to destroy all of your specimens that are still at the central laboratory.

How do we protect your privacy?

We will take every reasonable step to keep your health information private and to keep anyone from misusing it.

Your information (data) and samples will not be identified by name, or in any other way, in anything published about this study.

We will do everything we can to keep your personal information private, but we cannot guarantee that nobody will get it. We may have to release your personal information if required by law.

These people may see your medical and research information:

- Advarra Institutional Review Bboard (Advarra IRB);
- The sponsor, the group paying for the research (US NIH), other study research staff and study monitors
- US and other participating countries' health regulatory agencies, including the US FDA

They are committed to protecting your privacy.

As the research staff at the study site, we are required to make sure that people not involved with this study cannot see your research and medical information. We will keep your research files in a safe place and will handle your personal information very carefully.

Your study data are sent electronically to the UMN in the US through a secure system. By signing and dating this consent, you agree to having your data sent to UMN. No information that could directly identify you is sent to UMN. This is called "pseudonymized data". Access to the data at UMN is limited through security measures, and no data breach or unauthorized access has ever occurred in this system. After the study is over, the data will be stored securely for the period required by law.

Your study data will be shared with the US National Institutes of Health (which is paying for this study), and with regulatory authorities that oversee the study, including the US FDA, as required by law. Your study data will also be shared with the drug company that provides the study drug to help them develop the drug.

UMN may share your data and specimens with other people who study COVID-19. UMN will remove any information that could possibly be used to identify you before sharing. This is called "anonymizing the data." We will not ask you for additional consent for this sharing. UMN will only share data and specimens for research projects that are approved by the group that is conducting this study.

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.

This study has a Certificate of Confidentiality from the US Federal Government. This means that UMN cannot share any data it has about you with national, state, or local civil, criminal, administrative, legislative, or other authorities unless you specifically allow us to share it, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the agency which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:

  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046

- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00045358.

SIGNATURE PAGE FOR CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

I have read the consent or have had it explained to me. I believe that I understand the information. By signing and dating this consent, I am stating that I want to join this study. I understand that I do not waive any of my legal rights as a study subject by signing and dating this consent. I understand that I will receive a copy of the signed and dated consent.

If you agree to be in this study, please sign and date below.

_____ Date: _____
Signature of subject

_____
Printed name of participant

_____ Date: _____
Signature of study doctor/designee

_____
Printed name of study doctor/designee

FOR ADULTS NOT CAPABLE of GIVING CONSENT

_____ Date: _____
Signature of Legally Authorized Representative (LAR)

_____
Printed name of Legally Authorized Representative

_____
Relationship of Legally Authorized Representative to Subject

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under state or applicable local law)

Witness to Consent Interview

On the date given next to my signature, I witnessed the consent interview for the research study named above in this document. I attest that the information in this consent form was explained to the subject, and the subject indicated that his/her questions and concerns were adequately addressed.

_____ Date: _____

Signature of witness

_____

Printed name of witness

NOTE: This consent form, with the original signatures, MUST be retained on file by the Investigator of Record. A copy of the signed and dated consent must be given to the participant. A copy should be placed in the participant's medical record, if applicable.