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 H3: BRII-196/ BRII-198)

24 November 2020

NCT05780424

Informed Consent Form

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

Why are we doing this study?

We are studying a type of experimental drug called neutralizing monoclonal antibodies (nMAbs). This general type of medicine has been approved to treat many other diseases, but is early in development for treating COVID-19. 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 kind of experimental drug can help people in the hospital with COVID-19 get better and go home faster. We are also trying to see if it is safe.

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.

We are testing more than one type of nMAbs. If you join the study, you will be assigned by random chance - like flipping a coin or rolling dice - to get one of these nMAbs or a placebo. You could be in any of the groups below:

- VIR-7831, made by Vir Biotechnology, Inc. & GSK
- BRII-196 + BRII-198, made by Brii Biosciences
- Placebo (a salt water solution that has no active drug in it)

(If a study drug is marked out in the list above, it is because it is not available right now at your site.).

You will have an equal chance (1 in ___) of being in each group listed above. [Insert number of possibilities from the list above, including placebo, e.g. “3”]. This means your chances of getting an nMAbs drug instead of placebo are ___ out of ___. [Insert the number of active possibilities from the list above, then the total number of possibilities, e.g., “2 out of 3.”]

Your study doctor will not decide which group you are in, but you will both know which group you get assigned to. Neither you nor your study doctor will know whether you are getting an nMAbs drug or the placebo. No one on the study staff will know whether you are getting an experimental nMAbs drug or the inactive placebo. In case of an emergency, however, the study doctor can get this information.

We will tell you more about each study drug you could get in a separate consent addendum. You will be asked to sign and date the addendum for the study drug that you are assigned to take.

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 the study drug through an intravenous (IV) drip through a plastic tube attached to a needle in your arm. This is called an infusion. The separate information sheets will tell you how much liquid will be in the infusion and how long it should take to get it. It may sometimes take longer depending on how your body reacts to the infusion.

The nMAbs 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 (also called Veklury) for your COVID-19, unless your study doctor thinks remdesivir would not be safe for you to take. Remdesivir is given once a day by infusion for up to 10 days while you are in the hospital. Remdesivir was shown in an earlier study to help people get better more quickly from COVID-19. Remdesivir was recently approved by the US FDA and has approvals in many countries.

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 18 months. Most of the information we need to gather for the study will be recorded in the first 90 days.

We do not know what effects nMAbs may have on a pregnancy or unborn baby. There may be bad effects or no effects. If you decide to join the study, we strongly advise you to not have sex that could make you or a partner pregnant during the 18 months you are in the study. This may involve not having sex at all (abstinence), or you may use effective birth control (hormonal contraceptives like birth control pills or barrier methods with spermicide) to avoid pregnancy. Methods like rhythm, sympto-thermal or withdrawal are not considered effective for preventing pregnancy. You can ask the study team about this if you have questions or concerns.

If you become pregnant during the study, please let your study team know as soon as possible. The study team will collect information about your pregnancy and its outcome.

If you are male and your partner gets pregnant, we will ask your partner for consent to allow us to get basic information about her pregnancy.

You will also need to agree to not participate in any other COVID-19 study for the first 5 days you are in this study. There may be exceptions to this requirement. We will tell you about any studies you could participate in during the first 5 days of this study so you can make a choice.

This is what you will be doing for the study:

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] • 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	• 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)	• How you are feeling (Days 2, 4, 6, 7, 14, 60) • Update on return to home (Days 14, 42, 60, 75) These “visits” may take place by phone.	• How you are feeling • Blood for future research (18 mL, about a tablespoon) • On Day 28, also check whether you have taken certain medicines • Update on return to home

If you leave the hospital after just a few days, we will ask you to either come back, or else possibly be visited in your home by a professional working for the study 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.

After Day 90, we will contact you three more times by phone, at 6 months, 12 months, and 18 months, to see how you are doing and whether you have been in the hospital for any reason.

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

- By signing this consent, you agree to let us get information for this study from your medical record.
- By signing 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 some of the people in this study will get inactive placebo, and will not get any 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 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 work.

Why would you not want to be in the study?

Since only some of the people in this study will get the experimental drug, you may not get it. Even if you do get the experimental drug, it may not help, 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. The risk of the study drugs you may be assigned to are provided in a separate consent addendum for each study group. You should review the applicable addendum(s).

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

Getting nMAbs like the ones in this study may cause your body to release chemicals called cytokines. A cytokine reaction may have any of the symptoms listed above, as well as:

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

You will be monitored very closely while you are being given the infusion of the study product 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.
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. You will have these things done while you are in the hospital even if you are not in the study. You may have some pain, bleeding, or bruising when a needle is put into your vein to draw blood. Getting your nose swabbed can be uncomfortable and you might gag. These discomforts and risks are not very 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 not 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 NIH, an agency of the US Federal government, is paying for this study.

We are required to follow 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 1,000 subjects around the world for each nMAbs we are studying.

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 outside of the study 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 drugs, because they are 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 included abnormal liver function test results, abnormal blood clotting test results, constipation, nausea, vomiting, decreased appetite, and headache. The abnormal liver function tests lasted longer than a few days in some people, but went back to normal within a few weeks or less.

Remdesivir might affect the way that other medications are processed by your body. They might stay in your body longer, or shorter, at higher or lower levels. At the time this document was written, one person in this study had an increase in the level of a medication in their blood that was considered by study doctors to be at least possibly related to having taken remdesivir. There did not appear to be any harm from this temporary change. You can ask the study team more about this if you are concerned.

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 while you are getting remdesivir, 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 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 how much virus is 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 samples at any time. Let your study team know if you do not want the study to keep your samples anymore, and every effort will be made to destroy all of your samples 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 samples 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 samples 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.

A description of this clinical trial is also on the EU Clinical Trials Register (http://www.clinicaltrialsregister.eu/).

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 this consent or have had it explained to me. I have had a chance to learn about each of the nMAbs that I could be assigned to get. I have been given a copy of that information to keep. I believe that I understand the information. By signing and dating this consent, I am stating that I volunteer to join this study. I understand that I do not waive any of my legal rights as a study participant 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 participant

_____
Printed name of participant

_____ Date: _____
Signature of investigator/designee

_____
Printed name of investigator/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 Participant
(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 participant, and the participant 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.

Drug Information Sheet for TICO: BRII-196 and BRII-198

To accompany the informed consent for:

Therapeutics for Inpatients with COVID-19 (TICO)

Sponsored by: The University of Minnesota (UMN)

Funded by: The National Institute of Allergy and Infectious Diseases (NIAID), US National Institutes of Health (NIH)

Full Title of the Study: **A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients with COVID-19**

This information is about one of the experimental medicines you might be assigned to in the Therapeutics for Inpatients with COVID-19 (TICO) study. Like all of the medicines being studied in TICO, this is a type of medicine called neutralizing monoclonal antibodies (nMAbs).

BRII-196 and BRII-198 are two nMAbs that are given in two infusions, one right after the other. They are made by a company called Brii Biosciences (BriiBio). They were developed from a person who had recovered from COVID-19. Each nMAb works to try to block SARS-CoV-2, the virus that causes COVID-19. Each works on a different part of the virus.

BRII-196 and BRII-198 are given by intravenous (IV) infusion, through a plastic tube attached to a needle in your arm. The total volume of the two infusions is 200 mL (a little less than 1 cup).

As described in the study consent form, any drug, including nMAbs, can cause you to have an allergic reaction. This is the most common side effect seen with other nMAbs. Allergic reactions can be serious. An allergic reaction may have the following symptoms:

- 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)

PID: _____

Getting nMAbs like BRII-196 and BRII-198 may cause your body to release chemicals called cytokines. A cytokine reaction may have any of the symptoms listed above, as well as:

- fever
- muscle aches
- nausea
- vomiting, and/or
- headache.

It will take about an hour for you to get the infusions of BRII-196 and BRII-198. You will be monitored closely during the infusion and for a time afterwards. The speed of the infusion will be controlled to cut down the chance of a bad reaction. Medical personnel, equipment, and medication will be available in case you have a reaction.

This is the first study of these two nMAbs together in people with COVID-19. These nMAbs have been given separately to 12 healthy people in studies done by BriiBio. Three in each group took a dose lower than what we will use in this study, and the other 9 in each group got a dose higher than what we will use.

None of the people in these studies had any allergic reaction or cytokine reaction as described above. None of them had any side effects from the drug that were serious or life-threatening. Some people had abnormal laboratory values, but these returned to their usual level within 2 weeks. There did not appear to be any pattern to these abnormal values.

PID: _____