Protocol Name: Sarilumab for Patients with Moderate COVID-19 Disease: A Randomized Controlled Trial with a Play-The-Winner Design

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Informed Consent Version Date: December 11, 2020

ClinicalTrials.gov number: NCT04359901

1. Overview of the Research Study:

We are asking you to be in a research study that is being supported by the VA Boston Healthcare System. Before you decide to take part, you should know why the study is being done and what it will involve. This form tells you what to expect if you agree to be in the study. Taking part in this study is completely voluntary; it is your decision whether or not to participate.

We are doing the research to try to identify effective treatments for SARS-CoV-2 infection (also called "coronavirus infection" or "COVID-19"). The purpose of this research is to gather information on the safety and effectiveness of SARILUMAB (IL-6 receptor blocker) as an additional therapy for patients with confirmed SARS-CoV-2 infection and moderate respiratory symptoms. This anti-inflammatory medication has been FDA-approved to treat other illnesses, but we do not know yet if it is helpful for treating patients with COVID-19. By doing this study, we hope to learn if SARILUMAB is effective for reducing the severity of the disease caused by COVID-19. We will describe your involvement in more detail later in this form.

You might choose to volunteer in the study because we do not currently know what the best treatment regimen for SARS-CoV-2 is, and this study will help us find out if SARILUMAB improves outcomes for patients who have COVID-19 when given in addition to standard of care, which might include other medications and treatments. There is also the possibility that you may benefit from receiving the medication. You will find more information about benefits later in this form.

You may choose not to volunteer to be in the study if you are already feeling better without using this medication. You may also choose not to participate if you are worried about the risk of other infections, although other studies of short-term IL-6 inhibition do not show an increased risk. You will find more information about these risks later in this form.

Regardless of whether you participate in this study or not, you will receive the standard treatments that we provide all patients with SARS-CoV-2 infection and moderate to severe disease. You will find more information about alternate treatment/procedures later in this form.

Your doctor may also be an investigator in this research study. Being an investigator means your doctor is interested in both you and the study. You may want to get a second opinion about being in the study. You can do so now or at any time during the study. Another doctor who is not an investigator can give you a second opinion about being in the study. You do not have to agree to be in this study even though it is offered by your doctor.

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

2. WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study to compare usual treatments (also called "standard of care") with or without an additional anti-inflammatory medication called SARILUMAB for treating patients with moderate to severe illness caused by SARS-CoV-2. SARS-CoV-2 is a new infection that causes respiratory illness in some patients. It was first identified at the end of 2019, so we do not know very much about which treatments are and are not effective for treating it.

SARILUMAB is an anti-inflammatory medication that may help reduce some of the harmful effects of the SARS-CoV-2 virus. It is currently only FDA-approved for treating people with illnesses such as rheumatoid arthritis. We hope to learn if SARILUMAB improves outcomes for patients with SARS-CoV-2 infection or if the anti-inflammatory treatments are ineffective. Although risk of infection can occur with long-term use, other studies in patients with COVID have not shown an increased risk of infection with short-term use.

This study sponsored by the VA is being conducted at VA Boston Healthcare System and 4 other VA sites in the New England area. We expect to enroll approximately 120 participants.

You are being asked to participate because you have a confirmed SARS-CoV-2 infection and may have some new difficulty breathing or may require oxygen to help you with your breathing.

If you currently have a mild form of the disease, you may volunteer now in case you progress to a moderate form of the disease and you become eligible to be randomized (like a coin flip) to receive SARILUMAB or not.

3. HOW LONG WILL I BE IN THE STUDY? WHAT WILL HAPPEN AND WHAT CAN I EXPECT IF I TAKE PART IN THIS STUDY?

You will be in this study for 6 months if you choose to participate.

If you choose to participate you will be randomized (like a "coin flip") to receive either the standard of care, or the standard of care plus two injections of SARILUMAB. At the beginning of the study, an equal number of patients will be assigned to each group. As the study goes on, however, we may find that one group is doing better than the other group. If that is the case, then in later stages of the study, more patients will be assigned to the group that is doing better.

If you are assigned to the group that receives the study medication you will receive two doses that will be injected underneath your skin (a "subcutaneous injection"). If you are assigned to the group that

does not receive the study medication, you will not receive SARILUMAB. Both you and your doctor will know the group to which you are assigned and in either case, decisions about what other treatments you should receive will be made by your doctors outside of the research study.

Whether you receive a dose of SARILUMAB or not we will monitor your progress and collect information about your health from your medical record for a period of 6 months. There are no follow-up study visits required. Diagnostic testing may occur as part of your usual care for SARS-CoV-2 but will not be impacted by the study. No matter what you decide to do about joining the research study, you will receive standard treatments for patients with SARS-CoV-2 infection.

4. WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Since the medication being offered as part of this study is injected underneath your skin (a "subcutaneous injection") it may be uncomfortable or unpleasant to some people. You also may get some bruising or bleeding around the injection site.

As with any other medication, SARILUMAB may result in some side effects. There is a risk that the medication may lower the ability of your immune system to fight infections, although studies so far with short-term use in patients with COVID-19 have not found any increase in the rate of infection. When used in the long-term, drugs like SARILUMAB cause a small increase in risk of bowel perforation, meaning a hole in your intestine, which is a dangerous condition. This risk has been observed only in conditions in which the drug is given repeatedly over a long time period for a chronic disease and has not been found with one-time use among patients with COVID-19.

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

Because this is a new treatment strategy for SARS-CoV-2, we do not know all of its bad effects. You should contact Westyn Branch-Elliman, MD at pager 617-705-4348 if you have any bad effects. Off hours, you can call the West Roxbury VA page operator (857-203-3000) and request to speak to the physician on call for the medical service.

5. WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

Because SARS-Co-V-2 is a new infection, we do not know very much about the best ways to treat it. You are being referred to this study because it is possible that SARILUMAB, a medicine that reduces inflammation may improve outcomes in patients who have this infection. There is some data from other studies that suggests that SARILUMAB and similar anti-inflammatory medicines may be helpful, but we do not have enough data to know if they do or do not help to improve outcomes.

6. DO I HAVE TO TAKE PART IN THE STUDY?

Participation in this study is entirely voluntary. Regardless of whether or not you chose to participate, you will receive the standard-of-care treatment as offered by your doctors. There is no penalty or loss of benefits to which you are otherwise entitled if you choose not to take part in this study.

You may choose to withdraw from this study at any time. If you are receiving standard-of-care treatments or the study medication, the only difference would be that study investigators will not access your electronic medical record to find out some of the things that happened to you, like how long it took for your oxygen levels to improve.

If you do decide to withdraw from the study, any data that was collected before your withdrawal may be reviewed by study investigators. However, the only additional data investigators will be able to collect is from public records, such as survival data. Investigators will not be able to access other medical records data collected after your withdrawal, such as laboratory results or information about your oxygen levels.

7. WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

Other treatment to that described above may include available standard of care treatments and will be under the supervision of your doctor or caregiver.

8. HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Information collected for the purpose of this research study will be kept confidential as required by law. The results of this study may be published for scientific purposes, but your records or identity will not be revealed unless required by law.

Information about you is protected in the following ways: We will store your information in ways we think are secure. Data will be maintained on secure, password protected VA servers or on secure, password protected servers. The number of individuals with access to the data will be minimized and individuals no longer involved in research activities will have access to the secure server immediately revoked. Identifiable data will not be stored on desktops, laptops or jump drives.

Identifiers might be removed from the identifiable private information that are collected. After that removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative,

Your research records will be kept indefinitely or until the law allows their destruction per the VA Record Control Schedule (www1.va.gov/VHAPUBLICATIONS/RCS10/rcs10-1.pdf). Records will be destroyed, when allowed, in the following manner:

- Paper records will be shredded

- Electronic records will be destroyed in a manner in which they cannot be retrieved.

Your data will be entered into a data repository and may be used for future studies approved by an IRB.

An unsigned copy of this consent form will be posted on clinicaltrials.gov or Regulations.gov after all study participants have completed the 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.

9. WHO ELSE MIGHT SEE MY DATA?

You consent to the access of your VA research and medical records that may identify you by persons approved for this purpose. Such access may be by the Institutional Review Board and Research & Development Committees of VABHS, the VA, Federal agencies, or national research oversight and accreditation organizations. You understand that because this research study involves things that are regulated by the FDA they may choose to access and inspect your records.

You may expect the same confidentiality from these persons that is given to you by the Investigator and his/her research staff.

10. WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

You will be told of any significant new findings that come to light during the course of this study and that may relate to your wanting to stay in the study.

11. WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

A participant will not be required to pay for medical care and services received as a participant in an approved VA research study. Some participants are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services (including, but not limited to, dental services, supplies, medicines, orthopedic and prosthetic appliances, and domiciliary or nursing home care) provided by the VA that are not part of this research study.

12. WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

A new public health law under the Public Readiness and Emergency Preparedness Act (PREP Act) was issued by the Department of Health and Human Services on March 10, 2020. This law limits your

ability to sue if you are in a COVID-19 research study. If this study uses a drug, device or vaccine designed to treat, diagnose, cure or prevent COVID-19, you cannot sue the manufacturers, the study sponsor, healthcare providers or other professionals involved in the study for injury or harm (i.e., getting hurt) unless the injury or harm was on purpose. You may be compensated for injury or harm through a Department of Health and Human Services program called the Countermeasures Injury Compensation Program (CICP). For more information about this program, please contact the Health Resources and Services Administration's CICP by phone at 855-266-2427 or online at https://www.hrsa.gov/cicp/about/index.html.

VA will provide necessary medical treatment should you be injured by being in this study. You will be treated for the injury at no cost to you. This care may be provided by the local VAMC or arrangements may be made for contracted care at another facility. In case of research related injury resulting from this study, you should contact your study team. If you have questions about medical treatment for any study related injuries, you can call the operator at this VA Medical Center and ask for medical administration.

You still have the right to hold VA responsible for negligence that is not related to a COVID-19 research study.

13. WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

I understand that if I have any medical questions about this research study, I can page **Dr. Westyn Branch-Elliman,** at **617-705-4348** during normal working hours.

I understand that if I have any general questions about this research study, I can page **Dr. Westyn Branch-Elliman,** at **617-705-4348** during normal working hours.

I understand that if I have any medical problems that might be related to this study that **during the day** I can page **Dr. Westyn Branch-Elliman, MD** at **617-705-4348. After hours I can call the Medical Center operator at (617) 323-7700 and ask for the resident, fellow, or attending on call for Medical Service.**

I understand that, if at any point during or after this study I have any questions about my rights as a research participant or I want to discuss problems, complaints, concerns, and questions about the research, obtain information, or offer input, I may contact the Research Compliance Officer at (857) 364-4182.

14. AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

I have read or have had read to me all of the above. Study staff have explained the study to me and answered all of my questions. I have been told of the discomforts and risks of the study. I have been told of other choices of treatment that I could have.

I understand that my participation in this study is voluntary, that I do not have to take part in this study and that, if I do take part, I may withdraw from the study at any time. I also understand that, if I refuse to take part or if I decide to withdraw, I will not suffer any penalty, loss of rights, or loss of VA or other benefits that I have a right to receive.

I voluntarily consent to be in this study. I will receive a signed copy of this consent form.

Participant's Signature	Month	Day	Year	Name (print)

Signature of Participant's Legally Authorized Representative	Month	Day	Year	Name (print)

Signature of Witness	Month	Day	Year	Name (print)

Signature of Person Obtaining Consent	Month	Day	Year	Name (print)