REGENERON

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AS MODIFIED
Jun 24, 2020

GLOBAL STUDY LEVEL INFORMED CONSENT FORM (ICF)

TITLE: An Adaptive Phase 2/3, Randomized, Double-Blind, Placebo-Controlled Study Assessing Efficacy and Safety of Sarilumab for Hospitalized Patients with COVID-19

PROTOCOL NO.: 6R88-COV-2040
WIRB® Protocol #20200610

SPONSOR: Regeneron Pharmaceuticals, Inc.

INVESTIGATOR: Name
Address
City, State Zip
Country

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

NCT	NCT04315298
Site Number	[Site Number, if applicable]
Participant's Printed Name:	

Throughout this document, "you" and "your" includes the case where a Legally Authorized Representative is consenting on behalf of a patient.

In medicine there are many unanswered questions. A research study is when scientists try to answer a question about something that we don't know enough about. Participation in a research study may or may not directly help you or others. Participation is entirely voluntary. It is completely up to you whether or not you take part. You can also change your mind at any time and it will not affect your ability to get medical care within the [Institution Name].

The purpose of this research study is to determine if the investigational study drug sarilumab is safe and if it can decrease the amount of time you have COVID-19 symptoms.

If you choose to participate, you will be in this study for up to 60 days or until discharge from the hospital, and you may receive the investigational study drug or a placebo. Your alternative is not to participate.

The main risks to you if you choose to participate are infections. Common colds and urinary infections are the most common side effects reported in patients participating in sarilumab clinical studies. You can also experience oral herpes (cold sores), more serious infections, allergic reactions, and low white blood cell counts when using sarilumab. Unknown side effects may also occur.

Participating in this research may or may not benefit you.

If you are interested in learning more about this study, please continue to read below.

THE INFORMED CONSENT PROCESS

You are being asked to participate in a clinical research study sponsored by Regeneron Pharmaceuticals, Inc. ("**Regeneron**"). Your participation in this study is entirely voluntary.

This study involves research and is conducted to determine the safety and effectiveness of a study drug called sarilumab.

Sarilumab is currently being studied for treatment of COVID-19. You may be eligible to participate in this study if you meet certain requirements. Before you decide to participate, you need to understand the purpose of the study, the possible risks and benefits, and what would be expected of you. This process is called Informed Consent.

This document is an Informed Consent Form. Please read this entire document carefully. Take time to ask the study doctor or study staff as many questions about the study as you would like. If there are any words or information in this document that you do not understand, please ask the study doctor or study staff to explain them to you. You can also ask for a copy of this unsigned form to review with your physician, friends, and family.

If you agree to participate in this study, you must sign and date this consent form before any study-related tests or procedures are performed. A copy of the signed and dated document will be given to you.

To protect your safety, rights, wellbeing, and dignity, all information from the study is reviewed by an independent group of people called an Institutional Review Board (IRB). This study has been given a favorable opinion.

The Sponsor is paying for your care related specifically to this study and the study doctor will be paid by the Sponsor for those specific aspects of your care.

WHAT DOES THIS INFORMED CONSENT FORM DESCRIBE?

This document describes:

- The purpose and procedures of the study.
- Possible risks and side effects that you may experience.
- Possible benefits that you may experience from participation in this study.
- Other treatments or procedures (other than the procedure or treatment that is part of this study) that are available to you.
- How your personal and health information will be used and disclosed in this study and requests your permission for that use and disclosure.
- Your privacy rights in connection with the personal information collected from or shared by you in connection with the study.
- What compensation and/or medical treatment is available to you if injury occurs.
- Whom you can contact if you have questions about the study.
- Your rights as a research participant.

WHAT IS THE PURPOSE OF THIS STUDY?

You are being asked to participate in a research study of the investigational drug, sarilumab (study drug) sponsored by Regeneron Pharmaceuticals, Inc. (**"Regeneron"**) because you have the COVID-19 virus. This research study will be referred to as the "**study**" throughout this form.

Sarilumab (also known as Kevzara®) is considered an investigational drug in this study because it has not been approved for marketing by any health authority for the condition being studied but it has been approved in multiple countries for active rheumatoid arthritis.

Sarilumab is a type of drug called a "monoclonal antibody". An antibody is a special kind of protein that your immune (defense) system normally makes to fight bacteria and viruses. Scientists can now make antibodies in the laboratory and produce them for the treatment of many different diseases. Sarilumab has been specifically shown to block the action of a protein called interleukin-6 (IL-6) in your body. Interleukin-6 (IL-6) is a protein in the immune system that has been shown to play an important role in inflammation. Inflammation may be associated with complications of COVID-19.

The main purpose of this study is to determine if sarilumab is safe and if it can decrease the amount of time you have COVID-19 symptoms.

Regeneron, its collaborators or those developing the study drug; and their affiliates, representatives, agents and contractors (together, the "**Regeneron Parties**"), will use the information from the study to better understand the following:

- Side effects that may be experienced by people taking sarilumab
- How sarilumab works in the body
- How much sarilumab is present in your blood
- To see if sarilumab will decrease the amount of time you have COVID-19 symptoms

This document describes what is known about the study drug and study tests at the time this consent form is signed. You will be told in a timely manner if any important new information is learned during the conduct of the study that may affect your decision to take part in the study. Your participation in this study is entirely voluntary and you may withdraw from the study at any time. You do not need to give a reason, and your medical care (outside of the study) will not be affected by your decision.

After you sign this document, testing will be done to determine if you are eligible to participate in this study. You must meet certain requirements to be able to participate in this study. The study doctor will review all of the restrictions and requirements of the study with you to determine if you qualify for the study. There is a chance that you may not qualify. There is also a chance that you may qualify for the study but may not be able to participate due to other reasons such as the timing of enrollment.

WHAT WILL HAPPEN IF YOU JOIN THIS STUDY AND HOW LONG WILL IT LAST?

This is a randomized, double-blind, placebo-controlled study. "Randomized" means that the group you will be placed in is decided by chance, similar to drawing numbers out of a hat or flipping a coin. "Double-blind" means that neither you nor the study doctor will know which treatment group you have been placed in (ie, if you are receiving sarilumab or placebo). This is done to make sure the results of the study cannot be influenced by anyone. If there is an urgent need, the study doctor can find out quickly which study drug you are receiving. A placebo is an inactive substance, that looks like the medicine, but which contains no medicine. If you agree to take part in this study, you will receive either sarilumab or placebo.

Your participation in this study may last up to 60 days or until you are discharged from the hospital. This study consists of:

- A screening visit (1 day)

- A baseline visit (1 day), this can occur at the same time as the screening visit, if necessary.
- Monitoring period (58 to 59 days) or until discharged
- Follow-up telephone call on day 29 (if you are discharged before day 29) and at day 60

HOW BIG IS THE STUDY?

This study will include about 2300 patients at research centers in the United States. Due to the status of the current outbreak of the COVID-19 virus, the study may continue enrolling patients unless the study drug is shown to not work or not be safe for patients with COVID-19.

HOW WILL I BE GIVEN THE DRUG?

The study drug or placebo will be given through a vein (intravenous [IV] infusion). The infusion will last for about 1 hour. From here on, sarilumab and placebo will be referred to as the "study drug".

You will be given the study drug on day 1. If your COVID-19 symptoms do not improve, you may be given another dose on day 2. Then you may also be given the study drug on a weekly basis (up to 4-6 doses) until your COVID-19 symptoms improve or you are discharged from the hospital.

If you were enrolled into cohort 1, before April 27, 2020, you were randomly assigned to 1 of 3 possible study treatments (200 mg or 400 mg of sarilumab or placebo, IV, single or multiple doses).

If you are enrolled into cohort 1 after April 27, 2020, you will be randomly assigned to 1 of 2 possible study treatments (400 mg of sarilumab or placebo, IV, single or multiple doses).

- If you were in the 200 mg study treatment group and have not reached the 6-dose maximum, your study drug will be discontinued, and you will continue to be monitored until you are discharged from the hospital and have your follow-up telephone call(s).
- If you are on a ventilator and were in the placebo or 400 mg study treatment groups and you have not reached your 6-dose maximum, you will continue study treatment during the monitoring period as long as you are still on the ventilator. If you are no longer on a ventilator, your study treatment will be discontinued (if you have not already reached your 6-dose maximum) and you will continue to be monitored until you are discharged from the hospital and have your follow-up telephone call(s).

If you were in the placebo or 400 mg group, based on the severity of your disease when you enrolled into the study, the study doctor and sponsor may have you discontinue the study drug. You will continue to be monitored until you are discharged from the hospital and have your follow-up telephone call(s).

If you are enrolled into cohort 2 or 3, will be assigned to 1 of 2 possible study treatments.

You will be given either:

- 800 mg of sarilumab, IV, single or multiple dose (up to 4 doses maximum)
- Placebo, IV, single or multiple dose (up to 4 doses maximum)

The study will no longer enroll and give study drug to patients who are not on ventilators as of 06 June 2020. This change was made because patients who were not on a ventilator did not respond to study treatment, and among these patients, there were more deaths in patients who were receiving sarilumab than placebo. While these deaths could be due to COVID-19 and not sarilumab, patients not on a ventilator will no longer be enrolled or be given the study treatment. If you are not on a ventilator, your study drug will be discontinued, and you will continue to be monitored until you are discharged from the hospital and have your follow-up telephone call(s).

A data monitoring committee, that is not part of Regeneron, reviews safety and efficacy data from the study. This committee has recommended, and Regeneron agreed, that study drug can continue to be given to patients who are on ventilators.

The study staff will try to use the already established IV catheter line that was given to you for fluids to administer the study drug. There may be a chance that this is not possible, and the study staff will have to insert a new IV catheter line for the study drug.

Sarilumab has been approved for subcutaneous (under the skin) use. This is the first study where 200 mg, 400 mg and 800 mg IV infusion will be given to human volunteers and the first study in which the 400 mg and 800 mg dose levels will be used.

WHAT ELSE DO I HAVE TO DO WHILE PARTICIPATING IN THIS STUDY?

Some of the study procedures listed below are also part of your standard-of-care that you will receive while in the hospital, these procedures will not be repeated if your nurse had already performed them. The study staff will instead record the results from your chart. There may be times that the study staff may have to perform some of the procedures below if they had not already been done. These procedures will occur at different times during your hospital stay and may occur more than once in a single day. You can talk to the study staff if you have any questions about how and when these procedures will occur.

Questions/Information Collected About Your Health

The study staff may either ask you or collect the following information from your charts (if available): how you feel, current health status, your age, race, ethnicity, medical and surgical history, your food intake, smoking and alcohol habits, menopausal history (women only), physical activity, sexual habits or behavior, contraception and previous and current medications.

The study staff may collect the results from any tests run on biological samples (blood, urine, etc) taken from you, chest X-rays or imaging scans that were performed on you while you are in the hospital. The study staff will also collect information about any procedures done on you in relation to the COVID-19 virus.

Follow-up Call

If you are discharged from the hospital before day 29, the study staff will call you for a follow-up to check on your health status. You will receive a 2nd follow-up telephone call on day 60 to check on your health status again.

Electrocardiogram

An electrocardiogram (ECG) may be done. An ECG records electrical activity of your heart. For ECG recordings, a few sticky patches, called electrodes, will be placed on your chest.

Blood Draws

Study-related blood samples will be taken at different times during your participation in the study. The study staff will work with your doctor and nurse to ensure that, when possible, blood samples for this study are being taken at the same time as your standard-of-care blood samples are being taken and that samples are not accidently taken twice. See section "**What types of tests will be done during the study?**" for more information on blood samples.

Vital Signs

The study staff will take your vital signs, which will include measuring your blood pressure, pulse rate, and breathing rate.

Body Temperature

Your temperature may be measured from but not limited to your mouth, rectal, ear, or forehead.

Oxygen Level Measurements

Your blood-oxygen level (the amount of oxygen in your blood) will be measured by using a small device that will be placed on your index or middle finger.

The study staff will also record the amount of the oxygen that your body is absorbing from the devices that are being used to supply you with oxygen. You will not have to do anything for these tests to be done.

Physical Exams

A physical exam is a test used to check your overall health. Your weight will also be taken.

Pregnancy Test

If you are a woman of child bearing potential, a blood or urine pregnancy test will be required at screening.

Mouth, Nose and/or Throat Swabs

During the study, a swab of your mouth, nose and/or throat area may be done to test for COVID-19 virus and potentially for other types of infections. The study staff will determine the best location depending on your health.

WHAT ARE THE RISKS ASSOCIATED WITH THIS STUDY DRUG AND STUDY PROCEDURES?

The risks involved in giving sarilumab intravenously (given through a vein) are not fully known. There are known and predictable discomforts and common risks or side effects that you might experience with the use of the study drug or study procedures, including a decrease in neutrophils, a type of white blood cell that helps fight infection. There may be other risks not yet known when you take the study drug alone or when it is used with other medications. If important information is learned during the study which might affect you or make you change your mind about being in the study, the study doctor will tell you. The study doctor is trained to take the right measures to reduce risks and limit any discomfort you might feel. If you need more information, please ask your study doctor.

Risks Involved with the Study Drug

Risk for Infections

Because sarilumab may lead to a significant decrease in neutrophils (a type of white blood cell that helps fight infection), there is a chance that you could get a new infection after taking the study drug, even for 60 days after taking the drug or possibly longer. There is also a chance that your COVID-19 infection may last longer because of the study drug. See section "**What are the side effects associated with the study drug**" for more information on what types of infections have been experienced by patients who have taken sarilumab.

The information on infections with sarilumab is based on patients who have received lower doses under the skin every 2 weeks for long periods of time. This study will give a higher dose of sarilumab IV either as a single dose or multiple doses. You will not be given additional doses of the study drug if your neutrophil count is below a certain level.

Unforeseeable Risks

It is possible that there will be other side effects associated with sarilumab which are unknown at this time, some of which may be serious or life-threatening.

You should tell your nurse and/or study staff about any new health problems that happen while you are in this study and about any new medications you start taking (including vitamins and minerals, herbal remedies, over-the-counter drugs, and prescription drugs).

There may be unknown risks or side effects to an unborn baby or nursing child. You should not become pregnant or breast-feed while taking part in this study.

Risks Involved with the Study Procedures

Answer Questions About Your Health

These questions may make you uncomfortable.

Follow-up Call

There are no expected risks from the follow-up call.

Electrocardiogram

Sometimes it may hurt or produce slight pain when sticky patches placed on your chest are removed. In some people, these electrodes may cause slight irritation or redness of the skin in which goes away without any treatment.

Blood Draws

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and/or irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for a blood transfusion.

Vital Signs

The inflation of the blood pressure cuff may cause discomfort.

Body Temperature

There may be slight discomfort when your temperature is measured in the ear or rectum. There is no discomfort expected when taking your temperature from your mouth or forehead.

Oxygen Level Measurements

There are no expected risks or pain expected for taking blood oxygen levels.

Physical Exams

There are no expected risks or pain expected for performing physical exams.

Pregnancy Test

There are no expected risks or pain expected for performing a urine or blood pregnancy test.

Mouth, Nose and/or Throat Swabs

The swabbing of your mouth, nose and/or throat may cause mild temporary pain/discomfort in the area swabbed.

WHAT ARE THE OTHER TREATMENTS AVAILABLE FOR MY ILLNESS OR CONDITION?

Currently, there are no approved treatments for COVID-19, but the FDA may allow certain medicines to be used during the pandemic for COVID-19. You can choose not to participate in this study and receive standard of care medication currently used to try to treat viruses like COVID-19. Or you can volunteer in other COVID-19 clinical trials occurring at this hospital, if there are any available.

If you have any questions about alternative treatments, please ask your doctor. You and your doctor can decide what is best for you.

WHAT TYPES OF TESTS WILL BE DONE DURING THE STUDY?

Up to 3 tablespoons (approximately 40-45 mL) of blood may be drawn, at certain visits, during the study to run blood tests to check your overall health and disease-related tests.

The following will be tested at different times: drug concentration, study related biomarkers, including protein and virus in your blood and safety testing (if applicable). A blood or urine pregnancy test may be performed.

Blood samples will also be taken to monitor your safety and for possible infections by your doctor.

Additional blood and swabs (mouth, nose and/or throat) for research relating to measuring the study drug and how it works in your body as well as information about the amount of virus in your body may be collected.

WILL ADDITIONAL SAMPLES BE COLLECTED?

As described in this consent form, biological samples, including blood and mouth/nose/throat swabs will be collected as part of this study. Your coded samples will be used by Regeneron Parties for the purposes of the study, including exploratory research, to identify new learnings, such as:

- How the study drug works in the body;
- What makes some people respond better to the study drug;
- Why some people develop side effects;
- How the study drug or other related medications could affect COVID-19 and related viruses or conditions.

These samples will be stored in a secure storage space, at Regeneron Pharmaceuticals, 777 Old Saw Mill River Rd., Tarrytown, NY 10591, USA, for up to 15 years following completion of the study for the research purposes described in this consent form, unless you withdraw your consent to store your samples. Your samples will only be analyzed by Regeneron Parties. After 15 years, your samples will be destroyed. Identifiers might be removed from your identifiable private information or identifiable biospecimens and after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

If you wish to withdraw your consent to use and store your samples, please notify the study doctor in writing. If you withdraw from the study, but do not withdraw your consent to use and store your samples, your samples will continue to be used as described in this form. If you withdraw your consent to use the sample and you wish to have the samples destroyed, your study doctor, Regeneron, and the laboratory responsible for processing the samples will make every reasonable effort to ensure your samples are destroyed. However, it is important that you understand that if your sample has already been processed and analyzed, the results and information obtained cannot be destroyed and will continue to be available to the Regeneron Parties.

You should also know that it is possible that products may someday be developed with the help of your specimens and data, and there are no plans to share any profits from such products with you, regardless of whether your identifiable information is removed.

WILL THIS STUDY BENEFIT ME?

You may or may not benefit from your participation in the study. If the study drug is effective, and you are randomized to receive the study drug, it is possible that you may benefit by reducing the amount of time you have symptoms related to your COVID-19 infection.

However, your participation will provide new information on the effects of sarilumab in people with COVID-19. As a result, the information from this study might help other people like you in the future with COVID-19 or other viruses.

WHAT ARE THE SIDE EFFECTS ASSOCIATED WITH THE STUDY DRUG?

Sarilumab has been generally well tolerated by patients with rheumatoid arthritis. However, sarilumab has not been studied in patients with the coronavirus infection. There is always a chance that you may experience some side effects. It is important that you tell the study staff about these possible side effects.

Expected side effects, based on the experience from the studies of patients using sarilumab include the following:

Infections

Infections, mainly common colds and urinary infections are the most common side effects reported in patients participating in sarilumab clinical studies. You can also experience oral herpes (cold sores) when using sarilumab. At this time, infections are the most common serious side effect reported in patients who have been in sarilumab clinical studies. Treatment with sarilumab may increase the risk of a serious infection including tuberculosis (TB), due to the fact that your immune system may become weaker and not be able to fight infections caused by bacteria, fungi, or viruses. Rarely, the serious infections can be life-threatening (eg, sepsis) and may cause death. A few examples of serious infections experienced by study patients include pneumonia, skin infections called cellulitis, and shingles (a painful skin rash caused by the chicken pox virus). A few patients have had severe infections quickly develop after minor skin injuries (bruise or cut).

At any time after starting the study, if you have any new infection(s) or symptoms of infection(s), or if you injure yourself, have any kind of skin damage or skin wound, sore, or skin ulcer, you or your caregiver should immediately notify the study doctor.

Here are some examples of new symptoms you might feel if you have an additional infection for which you or your caregiver should immediately notify the study doctor:

- Fever, sweats, chills
- Muscle aches
- Feel like you are coming down with the flu or feeling generally ill
- Feel very tired
- Warm, red, swollen, or painful skin
- Diarrhea, vomiting or stomach pain
- Difficulty breathing, cannot seem to “catch your breath”, pain when you breathe, persistent coughing or coughing up blood
- Thick mucus coming from your lungs
- Hoarseness, runny or stuffy nose, or sore throat
- Burning, or pain when you urinate or urinating more often than normal for you
- Sudden or severe headache

Here are some examples of the types of skin injuries and skin rashes for which you or your caregiver should immediately notify the study doctor:

- Skin cut, scrape, tear, scratch, or an abrasion (for example a "skinned knee") other than as a part of your medical care
- Skin ulcer(s) or open sores on your body
- Sores or bumps on your skin filled with pus (collection of yellow-white fluid)
- Blisters, peeling skin or red skin rash
- Sores or white patches on your lips, mouth or tongue
- Bruised, punctured, or torn skin on hands, feet, arms or legs

Allergic Reactions (hypersensitivity reaction)

Allergic reactions (sometimes severe, or in rare cases, fatal) have occurred with other biologic products that are similar to sarilumab. There have been a few reports of allergic reactions after sarilumab was given. These reactions were described as mild and moderate allergic reactions (for example, hives and swelling in the face), so you may experience skin rash, or rash with red, raised, itchy bumps. In addition, there have also been rare cases of severe skin reactions in patients receiving sarilumab. Whether sarilumab caused these severe reactions could not be clearly determined.

Laboratory abnormalities

- Low white blood cell count
- Low neutrophil blood cell count (the neutrophil is a type of white blood cell, that helps fight off infection). A decrease in neutrophil count was not associated with the occurrences of infections, including severe infections.
  In most cases of patients who experienced a drop in neutrophil counts with subcutaneous administration of sarilumab, the neutrophil cell counts increased when dosing was interrupted without additional medical problems or complications. However, the duration of low neutrophil cell counts following intravenous administration of sarilumab is not known and may be longer compared to subcutaneous administration.
- Elevation in cholesterol, including LDL and HDL and/or elevation of triglyceride. Risk of heart problems or stroke may increase due to LDL increase. If this happens, your doctor might recommend starting another medication to control your cholesterol. This may not occur in patients only receiving a limited number of doses of sarilumab.
- Elevations in liver function tests (these tests indicate inflammation in the liver).

- Low platelet count: a few cases of low platelet counts (without bleeding problems) were reported in patients using sarilumab. Risk of bleeding and bruising might increase due to low platelet count. Sometimes the low platelet count may be treated with a blood transfusion.

You may not receive additional doses of study drug if your neutrophil count is too low or certain liver function tests are too high.

For most people, their blood test results will return to normal after stopping sarilumab. In rare cases, the abnormal blood tests might be serious and may lead to a hospitalization.

Potential side effects, based on experience with long term use of sarilumab and other biologic medicines (which are usually given by injection or directly into the bloodstream) including an approved drug which works in the same way as sarilumab, include the following:

- A few cases of diverticulitis, small bulging pouches that form in the digestive tract and that can become infected, were reported in patients using sarilumab. Sometimes these infected pouches can cause small holes in the intestines causing a perforation (seen on a special type of X-ray called a CT [or CAT] scan). If you have had severe diverticulitis or an intestinal perforation, please report this information to your study doctor so he/she can determine if it is still safe for you to participate in the study.
- People with chronic inflammatory diseases, especially those with very active disease, may be more likely to get lymphoma and other types of cancer, such as that observed in rheumatoid arthritis patients. The risk of getting lymphoma or other cancers may increase with the use of other types of biological drugs since they affect immune system. Sarilumab may also decrease the activity of your immune system.

  To date, clinical studies have not suggested an increase in the frequency of cancer in patients treated with sarilumab.

Some of the potential side effects seen with long term use of sarilumab, as described above, may not be relevant for studies only using a limited number of doses of sarilumab.

It is also possible that there may be other risks that are not known at this time that can occur with the use of the study drug, including interactions with other medications.

Side Effects for Intravenous Infusion

The study drug will be given by IV infusion. You may bruise or feel pain or discomfort at the infusion site. Also, infusion related reactions (side effects) such as the following can occur within 2 hours after finishing the infusion:

- Nausea
- Vomiting
- Low or high blood pressure
- Headache
- Flushing (red cheeks)
- Swollen lips tongue and uvula (soft hanging palate between the tonsils in the mouth)
- Bronchospasm (constriction of the airways, with shortness of breath), or other acute pulmonary response
- Angioedema (swelling below the skin or eyelids or throat)
- Syncope (temporary loss of consciousness caused by a fall in blood pressure)
- Cardiac arrhythmias (irregular heartbeats)
- Tachycardia (increased heartbeats)
- Dizziness
- Dyspnea (difficulty breathing), chest pain
- Headache
- Malaise (general feeling of discomfort, fatigue, or uneasiness)
- Skin rash
- Itching or hives
- Seizure, other neurologic symptoms (confusion, loss of consciousness, paresthesia, paralysis)

There is also the potential for infiltration, that is when the study drug leaks out of the vein under the skin and causes swelling to the tissue around the IV site.

WHAT HAPPENS IF I GET INJURED WHILE I AM IN THE STUDY?

If you think you have been injured as a result of participating in the study:

1. Promptly seek medical treatment, and
2. Call the emergency contact number on the first page of this form.

If you have an injury that is directly caused by taking the study drug or any properly performed study procedures included in the study (procedures you receive only because of your participation in the study) and you have followed the directions of your study doctor, Regeneron will provide reimbursement for reasonable and necessary medical costs to treat your injury that are not covered by your medical or hospital insurance, or from third party or other programs providing such coverage.

Regeneron will not routinely provide monetary or financial compensation for:

- other injury- or illness-related costs (such as lost wages, disability or discomfort due to an injury),
- medical expenses that are paid for by a third party,
- medical expenses that happen due to a violation of the study or other misconduct or negligence, in each case by any agent or employee of the Institution conducting the study (including the study staff), or
- medical expenses for injury or illness unrelated to the study drug and unrelated to the proper performance of any other procedure required by the study or Regeneron's written instructions to the Institution conducting the study, including, without limitation, medical expenses associated with a pre-existing medical condition.

No funds have been set aside to provide you with any further monetary or financial compensation in case of injury.

By agreeing to participate in this study, you do not waive any of your legal rights.

This research is covered by the Public Readiness and Emergency Preparedness (PREP) Act. The PREP Act limits your ability to sue if you are injured by the study drug or study procedures. However, you may be able to seek compensation from the Health Resources and Services Administration (HRSA) Countermeasure Injury Compensation Program for certain serious physical injuries. The declaration is available at: https://www.govinfo.gov/content/pkg/FR-2020-03-17/pdf/2020-05484.pdf.

For more information, please contact the study doctor or a member of the study staff.

WHAT HAPPENS IF I GET PREGNANT?

It is possible that sarilumab may harm the unborn child. It is unclear what the effect of sarilumab is on a baby born from a mother that took sarilumab while she was pregnant. As of 12 Jan 2020, there were a total of 30 patients, including 6 male patients whose partners became pregnant during non-COVID studies. Two of the male patients had female partners who became pregnant twice. There were 18 full-term births, 9 miscarriages, 2 elective abortions and 1 pregnancy with an unknown outcome. Three of the patients with miscarriages had a prior history of miscarriages.

One patient delivered a baby who was diagnosed with pneumonia when born. The baby received treatment and recovered.

It is unknown if sarilumab is present the milk of breast-feeding mothers. It is known that monoclonal antibodies are excreted in small amounts in breast milk.

For Women

You will still be allowed to participate in this study even if you are pregnant or become pregnant during your participation. But, it is important that you do all that you can to not become pregnant and not to breastfeed while participating in this study. Please talk to your study doctor for approved methods of birth control that you can use during this study.

WILL I BE PAID TO PARTICIPATE IN THIS STUDY?

You will not be paid for participating in this study.

WILL I HAVE TO SPEND MONEY TO BE IN THIS STUDY?

There will be no cost to you for the study drug, study doctor's time or certain procedures and supplies required by this study.

You are responsible for the cost of your standard medication, in addition to any costs related to procedures and supplies not required by the study.

WHY WOULD I BE ASKED TO DISCONTINUE THE STUDY?

The study doctor or Regeneron can remove you from the study without your consent at any time for any reason including:

- To improve your medical care,
- If you experience unusual or serious side effects,
- If you do not follow the study procedures as instructed,
- If the study is stopped by Regeneron or a health/regulatory agency such as FDA, or
- Other reasons not listed here.

The same procedures will be followed as those that would happen if you decided to discontinue from the study.

DATA PROTECTION: YOUR RIGHTS AND CHOICES

WHAT INFORMATION WILL THE STUDY STAFF COLLECT FROM OR ABOUT YOU IN CONNECTION WITH THIS STUDY?

As part of this study, the study doctor and study staff ("**Researchers**") will collect and review information about you that contains your name and other personal information. In addition, your treating physicians and other healthcare providers may disclose information from your medical records to the Researchers. The information collected from or about you ("**Personal Information**") for this study includes:

- Your medical information, including how you feel, medical and surgical history, your food intake, smoking and alcohol habits, menopausal history (women only), physical activity, sexual habits or behavior, contraception and previous and current medications.
- Other personally identifying information, including your name and other information (such as your age, race or ethnicity, gender and country location).
- Results of examinations and laboratory tests.
- Biological samples (from the mouth, nose, and/or throat, blood, or other samples taken as part of your standard-of-care).

Access to your records, directly at the study site or remotely may be available to regulatory authorities, monitors, auditors, and representatives of the Sponsor at the study site for monitoring, auditing, and verification of research procedures and/or study data.

The Sponsor or its representatives may conduct site visits to monitor and ensure that the trial is executed according to the study protocol and applicable local laws and regulations.

WHO ELSE WILL BE ABLE TO LOOK AT MY PERSONAL INFORMATION?

The Researchers will use and disclose your Personal Information to the following organizations:

- Regeneron, its collaborators or those developing the study drug; and their affiliates, representatives, agents and contractors (the "**Regeneron Parties**")
- The U.S. Food and Drug Administration (FDA), other U.S. government agencies, and government authorities in other countries
- The Institutional Review Board (IRB), a group that looks out for the rights and welfare of research participants

Generally, your permission to use and/or share your Personal Information for the purposes described in this form does not have an expiration date, subject to applicable law, unless you withdraw your permission in writing to the study doctor at the address listed on page 1 of this form.

WHAT PRECAUTIONS WILL BE TAKEN TO PROTECT MY PRIVACY?

Every effort will be taken to maintain your privacy. Your name will not be attached to records or samples released for research purposes. Instead, your records and samples will only be identified by a code. Only the study doctor and authorized personnel will be able to connect this code to your name. Your Personal Information will be protected by your study doctor and site in accordance with relevant data protection laws.

All data will be stored in locked cabinet files and restricted-access computers. While these security measures reduce the risk of your personal information being misused or accessed by unauthorized individuals, such risks cannot be eliminated entirely. Although we believe that these risks are low, absolute confidentiality cannot be promised. However, all information will be collected and shared in accordance with applicable law and data sharing guidelines that the Sponsor must follow.

HOW WILL MY PERSONAL INFORMATION AND RESULTS FROM THIS STUDY BE USED?

The Researchers and organizations listed above will use and disclose your Personal Information in connection with the study to assure quality control, analyze the data, and comply with regulatory duties. This includes the submission of the study results, regulatory approvals of the study drug, to report adverse events, and government reporting, if applicable. In addition, Regeneron Parties will use the study data to assess the safety and efficacy of the study drug.

Your coded Personal Information will be added to a computerized database. This database will be part of the study results. Data and results from this study will be presented at meetings or published in journals. To fulfill regulatory requirements and industry guidelines, the results from this study will also be provided to qualified researchers who request it for legitimate research purposes. While your coded information may be shared with these researchers or publications, your identity (such as your name, address and email) will not be shared with these researchers and will not be in any presentation or publication.

As advancements in medical technology continue, Regeneron Parties may reanalyze the study data and the results in future research projects to find new scientific information about the study, study drug, COVID-19, or other related diseases.

Once your Personal Information is disclosed to the Regeneron Parties and to the other organizations identified above, it may be subject to further disclosure and no longer protected by federal privacy law.

WILL I HAVE ACCESS TO MY RESULTS?

The results produced as part of this study are for research purposes only. The results are not reviewed for medical diagnosis of any disease. Because the results obtained during the course of the research have only clinical research value and are not for medical diagnosis, the Sponsor does not provide individual results to you. In some circumstances, the Sponsor may provide certain results to your study doctor. If, during the course of the study, the study doctor learns information related to your health from the study procedures, the study doctor may discuss this information and your options with you.

WHAT ARE MY PRIVACY RIGHTS?

Your Right to Access and/or Correct Your Information

You have the right to access, through your study doctor, all of the information collected about you in your medical record, and to ask for corrections, according to the rules of the study site. You have the right to request information on how the Personal Information reported to the Sponsor are being used and with whom the data have been shared. Please note that your right to access certain information in your medical records may be suspended during your participation in the study. Therefore, if you would like immediate access to your records, you may not be able to continue participating in the study.

Your Right to Object/Withdraw

In order to participate in this study, the Sponsor must collect and use your Personal Information. Your decision to allow the collection and use of your health information is completely voluntary but if you do not allow it, you may not participate in the study. If you change your mind about your Personal Information being used, you can voluntarily withdraw from the study at any time. If you choose to withdraw your permission, you will not be punished in any way or lose any right to access care, treatment, or services outside of the study.

If you withdraw your permission to use your Personal Information, the Personal Information collected prior to your withdrawal will still be processed along with other data collected as part of the study in order to preserve the integrity of the results and in accordance with regulatory requirements. The information collected about you up to the point when you discontinue from

the study, or information obtained after you withdraw in connection with a safety issue related to the study, will continue to be used, including lab results, clinic notes, and any other information collected. However, no new information will be collected unless you specifically consent to that.

Your Right to Request Deletion

If you withdraw from the study, you may also request that the Personal Information already collected from you in connection with the study be deleted. However, your right to deletion is limited due to regulatory requirements and to preserve scientific integrity, as your Personal Information must be managed in specific ways in order for the research to be reliable and accurate. The study results and coded data will be kept as long as they are needed for research purposes, any regulatory requirements, and the Sponsor's Data Retention Schedule.

Please be aware that because the Sponsor only maintains coded study data, it generally cannot respond directly to individual requests regarding your privacy rights. Therefore, you should address any of these requests regarding these rights to the study site using the contact information on the first page of this consent form. If you have any questions, concerns, or complaints as to how your **Personal Information** has been handled, you can contact the Sponsor's Data Protection Officer at DataProtection@Regeneron.com.

WILL MY INFORMATION BE ON THE INTERNET?

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 will also be available on https://www.clinicaltrialsregister.eu/. Some regulatory authorities and ethics committees may also make information available on their websites.

CAN I CHANGE MY MIND ABOUT BEING IN THE STUDY?

Yes. Your participation is voluntary. You may discontinue being in the study at any time. You do not need to give a reason and your medical care (outside of the study) will not be affected by your decision. Refusal to participate or discontinuing participation will not involve penalty or loss of benefits to which you are otherwise entitled.

If you decide to discontinue being in the study, you should let the study doctor know before you stop. If you have already taken the study drug, you will be asked whether you allow the Sponsor to continue to collect information about your health. You may be asked to provide a final blood draw sample before you withdraw from the study. You will be asked to allow the Sponsor to contact you for a follow-up call to ensure there have been no changes in your health.

If you would like to withdraw from the study completely without allowing the Sponsor to continue to collect additional information about you, you can do so by telling your study doctor.

WHAT IF SOMETHING IS DEVELOPED FROM THIS RESEARCH?

By participating in this study, you do not acquire any ownership rights in the samples you contribute or in any medical or genetic tests, drugs or other commercial products that may be developed through this research.

WHO DO I CALL IF I HAVE QUESTIONS?

The people to contact for any questions, concerns, complaints, a research-related injury, or problems in the study are listed on the first page of this consent. You may ask questions before you sign the consent, at any time during your participation in the study, and after you are finished with the study.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (800) 562-4789, help@wirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

Protocol Title:	**An Adaptive Phase 2/3, Randomized, Double-Blind, Placebo-Controlled Study Assessing Efficacy and Safety of Sarilumab for Hospitalized Patients with COVID-19**
Protocol Number: **Sponsor:** **Research Site:**	6R88-COV-2040 Regeneron Pharmaceuticals, Inc. [Site Name]

PARTICIPANT'S AGREEMENT

All subjects unable to consent are required to assent, unless the investigator determines that the capability of the subject is so limited that the subject cannot reasonably be consulted.

If assent is obtained, have the person obtaining assent document assent on the consent form.

- I have read and understand this Informed Consent Form (ICF). This study has been explained to me in detail and all of my questions have been answered to my satisfaction. I have been given enough time to decide whether I want to participate or not.
- I authorize the collection, use, disclosure and storage of my Personal Information and biological samples for the purposes of this study as described in this form.
- I volunteer to participate in this research study.
- I have been informed of my privacy rights related to the collection, use and disclosure of my Personal Information and consent to such collection, use and disclosure.
- I am free to withdraw my consent to the collection, use, and disclosure of my Personal Information at any time without penalty and without affecting my medical treatment; however, I will not be able to continue my participation in the research study after I withdraw consent, and data already collected will continue to be included in study analyses, in accordance with regulatory requirements.
- I agree that my GP/personal physician can be informed of my participation in this study.
- By signing this form, I have not waived any of the legal rights that I otherwise would have as a participant in a research study. I understand that I will receive a signed copy of this form for my records.

A copy of the information sheet and your signed consent form will be given to you to keep.

_____
Name of Participant (printed)

_____ _____
Signature of Participant Date (DDMMMYYYY)

LEGALLY AUTHORIZED REPRESENTATIVE AND PERSON OBTAINING CONSENT SIGNATURES

The Legally Authorized Representative signature should be added if the patient is unable to sign for himself or herself. The relationship between the patient and the Legally Authorized Representative should be stated.

_____
Name of Legally Authorized Representative (if applicable)

_____ _____
Signature of Legally Authorized Representative (if applicable) Date (DDMMMYYYY)

_____
Relationship of Legally Authorized Representative to Participant (Printed)

I have fully informed the participant/Legally Authorized Representative about the study:

- ❑ I have explained the study to the extent compatible with the subject's capability, and the subject has agreed to be in the study.

OR

- ❑ The subject is not able to assent because the capability of the subject is so limited that the subject cannot reasonably be consulted.

_____
Name of Study Investigator
Or Person Obtaining Consent/Assent

_____ _____
Signature of Investigator or Person Obtaining Consent/Assent — Date (DDMMMYYYY)

WITNESS SIGNATURE

- ❑ Not applicable, witness signature is not needed.
- ❑ Applicable – See witness signature and language below.

As an impartial third party, I witnessed the entire consent discussion. I attest that the above-named participant received a verbal and written description of the study. This individual had sufficient time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participate in this study.

_____ _____
Name of Witness (printed) — Date (DDMMMYYYY)

_____ _____
Signature of Witness — Date (DDMMMYYYY)

****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 <u>may</u> 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, 2070.

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/LAR	**Date**
Authority of LAR	