Official Title: A Phase II Trial to Evaluate the Safety and Tolerability of Clazakizumab® (Anti IL-6 monoclonal) compared to placebo for the treatment of COVID-19 infection

NCT #: NCT04348500

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CEDARS-SINAI MEDICAL CENTER

CONSENT FORM FOR RESEARCH

Title: A Phase II Trial to Evaluate the Safety and Tolerability of Clazakizumab® (Anti-IL-6 monoclonal) compared to placebo for the treatment of COVID-19 infection

STUDY SUPPORT PROVIDED BY: Vitaeris Inc.

PARTICIPATING RESEARCHERS:

STANLEY JORDAN, MD **PRINCIPAL INVESTIGATOR**

STUDY CONTACT PHONE NUMBER AT CSMC: 310-423-2641

AFTER HOURS CONTACT (24 HOURS): 310-423-2641

This research study is sponsored by Cedars-Sinai Medical Center. Vitaeris Inc. has provided Cedars-Sinai Medical Center with the medication for this study; Vitaeris Inc. is not providing additional compensation to Cedars Sinai Medical Center or the Principal Investigator for their participation in the study.

KEY INFORMATION ABOUT THIS RESEARCH STUDY

We are seeking your consent to take part in this research study. Your participation in this research is voluntary. If you choose to participate, you can stop at any time. Please consider the following summary, along with the more detailed information provided throughout this consent form.

- The purpose of this study is to investigate the effectiveness and safety of treatment with clazakizumab compared to a placebo (inactive substance). We are proposing to try this drug to treat your Coronavirus Disease 2019 (COVID-19) infection. Patients with COVID-19 infection have been shown to have increases in certain inflammatory processes. Clazakizumab is an antibody (immune system protein) that blocks certain inflammatory processes. The treatment plan is to attempt to inhibit or block these inflammatory processes in order to try to limit the damage COVID-19 causes to the lungs.
- The main procedures of this study include infusions of either clazakizumab or placebo given intravenously once. Neither you or the study doctor will know which treatment you are given. In addition, 24 hours to 14 days later you may receive a dose of clazakizumab, if your condition gets worse (you will be eligible for this option regardless of which group you are in for the first dose).
- All research studies involve some risks. Risks or discomforts from this study may include: Infections, Liver Function Test Abnormalities (elevated liver enzymes and hepatic events), Blood abnormalities, cholesterol and triglycerides abnormalities, gastrointestinal perforations.

- The study drug you are being given may or may not improve your COVID-19 disease. The knowledge gained from this study may also be of help to other patients in the future. However, there is no guarantee that you will benefit from this study.
- If you choose not to participate, there may be other choices available to you. You will not lose any services, benefits or rights you would normally have if you choose not to participate. Please discuss your choices with the researchers.

Please take time to read this entire form and ask questions before deciding whether to participate in this study. You are encouraged to talk with family members, close friends, trusted advisors and/or healthcare providers before you make your decision.

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

We are doing this study to examine the effectiveness and safety of treatment with clazakizumab compared to a placebo (inactive substance) in COVID-19 disease. Possible benefits of treatment of COVID-19 with clazakizumab include improvement in lung function (ability to breathe without assistance), reduced risk of worsening lung function, and reduction of fevers. However, the effectiveness of clazakizumab to treat COVID-19 has not been shown.

You are being asked to take part in this research study because you have a confirmed diagnosis of infection with COVID-19 disease with inflammation that is affecting your lungs.

The study will enroll approximately 60 people at one study site (Cedars-Sinai Medical Center).

This research study is designed to test the investigational use of clazakizumab. This drug has not been approved by the U.S. Food and Drug Administration (FDA). To date, over 1,000 people (healthy volunteers, patients with rheumatoid arthritis, psoriatic arthritis, Crohn's disease, graft-versus-host disease, advanced cancer, highly sensitized patients awaiting a kidney transplant, and antibody mediated rejection) have taken this investigational drug in clinical studies.

In this study, we want to compare clazakizumab to the control treatment placebo to learn whateffects, good or bad, clazakizumab has on people with your condition. We will give either clazakizumab or a placebo treatment to research participants and watch carefully for any side effects.. Neither you or the study doctor will know which treatment group you have been assigned to. In addition, 24 hours to 14 days later you may receive a dose of clazakizumab, if your condition gets worse (you will be eligible for this option regardless of which group you are in for the first dose).

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as an Appendix.

The flowchart shows a timeline for research-related or standard of care procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. **Standard of care**

(routine) procedures would be performed both as part of this study and if you do not participate in this study.

A table describing common medical procedures done solely for the purposes of monitoring and assessing your condition during this study is attached as an Appendix to the end of this consent form. Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart Appendix.

Overview of study:
This is a randomized, double-blind research study.

- "**Randomized**" means that you will be assigned to a study group by chance, like flipping a coin. You will be randomized into one of two study groups, and will have an equal chance of being placed in one of the groups described above.
- **"Double-blind"** means neither you nor the researchers will know what group you are assigned to.

This study has 2 study groups:

- Group 1 will get the receive an infusion of 25mg clazakizumab intravenously
- Group 2 will receive an infusion of a placebo (inactive substance) intravenously

Whether you are assigned to Group 1 or Group 2, 24 hours to 14 days later you may receive a dose of clazakizumab, if your condition gets worse.

A computer will randomly assign you to a study group. This is done because no one knows if the results experienced by the participants in one study group are better, the same, or worse than the results experienced by participants in the other. Once you are put in one group, you cannot switch to another group. Neither you nor your doctor can choose the group in which you will be placed.

In order to properly follow the study's protocol (research plan), all participants will receive treatments and procedures that have been pre-determined by the protocol. In effect, the protocol describes which medications or procedures you will receive, rather than those decisions being made by your personal doctor or based on your preference. There may be options available outside of this study that you will not be able to receive while participating in this study. There may be additional risks due to this limitation, such as the inability to receive other off-label or investigational drugs that are being used as part of clinical trials to see if they are effective at treating COVID-19 infection. You should discuss potential risks with your doctor.

A. Screening Period

During this period, you will be evaluated by your study doctor to see if you qualify to be entered into this study. Your study doctor will check which medications are acceptable for you to continue taking. If you are taking medications, herbal or traditional remedies, vitamins, hormones or dietary supplements, you should speak with your study doctor who will tell you if you must stop taking any of the medicines you are currently taking.

B. Treatment Period

If you meet all the study requirements and decide to participate, you will be randomly assigned (like flipping a coin) to receive either 25 mg clazakizumab or placebo (normal saline) by intravenous infusion once. The use of a placebo helps to make sure that any side effects and tests during the study are judged fairly. You will have a 50% (1 in 2) chance of receiving clazakizumab and a 50% (1 in 2) chance of receiving the placebo. Neither you nor your study doctor can choose the group you will be in. Neither you nor the study staff will know to which group you have been assigned, unless there is an emergency. The treatment period can last up to 14 days. During the 14 days after you receive clazakizumab or placebo, if your COVID-19 related disease worsens, the treating physician may determine that you need another dose of clazakizumab infusion. All patients who receive a "second dose" will get clazakizumab instead of placebo. You and your study doctor will still not know if you received clazakizumab or placebo for your "first dose." The study doctor must wait at least 24 hours before giving the second dose.

C. End of Study/Early Termination Visit

After completing treatment with study drug, or if your study doctor ends your participation early because of your health, or if you want to stop taking part in the study, you will be asked to undergo the End of Study Visit procedures.

D. Follow-up Period

After your last dose of study drug, you will receive one telephone call from your study doctor or study staff at 60 days. During this time, you will not receive any more study drug.

E. Screening (Visit 1)

The following tests and procedures will be performed to determine if you qualify to participate in this study.

- Review of your medical history and medication history. Your study doctor will also ask you questions about your alcohol and drug use.
- A full physical examination and measurement of your height, weight, vital signs (heart rate, blood pressure, breathing rate, and temperature)
- Tuberculosis screening – A blood sample will be collected, and a chest x-ray will be done. Active tuberculosis cases may be reportable to local health authorities according to local law.
- Pregnancy test for women of child bearing potential

F. Study Treatment (Day 1)

At this visit, you will be asked to read and sign this informed consent form before any study-related tests are performed. If you qualify to participate in the study, you will have the following tests and procedures depending on the visit:

- Complete physical exam including vital signs
- Blood sample collection for testing including interleukin 6 [also known as IL-6 which is a protein in your cells]; liver function tests (LFTs), complete blood count (CBC), inflammation markers, ferritin, D-dimer, troponin, procalcitonin

- Clazakizumab or placebo infusion

G. Study Treatment (Day 3 to 28)

If you qualify to participate in the study, you will have the following tests and procedures depending on the visit:

- Review of any side effects and changes to your medicines.
- Complete physical exam including vital signs
- Blood sample collection for testing including interleukin 6 [also known as IL-6 which is a protein in your cells]; LFTs, CBC, inflammation markers, ferritin, D-dimer, troponin, procalcitonin, clinical chemistry
- Up to study day 14, if a dose of clazakizumab is deemed necessary by your treating physician, you would receive one clazakizumab infusion (there would be no placebo infusion given during this time frame)
- Assessment of above labs and clinical chemistry collected by standard of care
- Assessment of Chest X-rays collected by standard of care, patient survival
- Assessment of use of proning
- Assessment of any other infections
- Assessment of the number of days from when symptoms began to the first dose of clazakizumab or placebo

H. End of Study (Day 60) or Early Termination Visit

At this visit, the following procedure will be performed:

- Phone interview to review any adverse events you have experienced since hospital discharge
- Assessment of any other antiviral agents during your hospitalization

This is a randomized, double-blind, Placebo controlled, Phase 2 single-center research study.

- "**Randomized**" means that you will be assigned to a study group by chance, like flipping a coin. You will be randomized into one of two study groups, and will have a 1:1 chance of being placed in one of the groups described above.
- **"Double-blind"** means neither you nor the researchers will know what group you are assigned to.

This is a placebo-controlled study. It will compare the effects (good or bad) of clazakizumab against the effects of a placebo (an inactive substance, such as, a sugar pill) on the condition being studied in this research. Another way to find out what will happen to you during the study is to review the figure below. Start at the left side and read across to the right, following the lines and arrows.

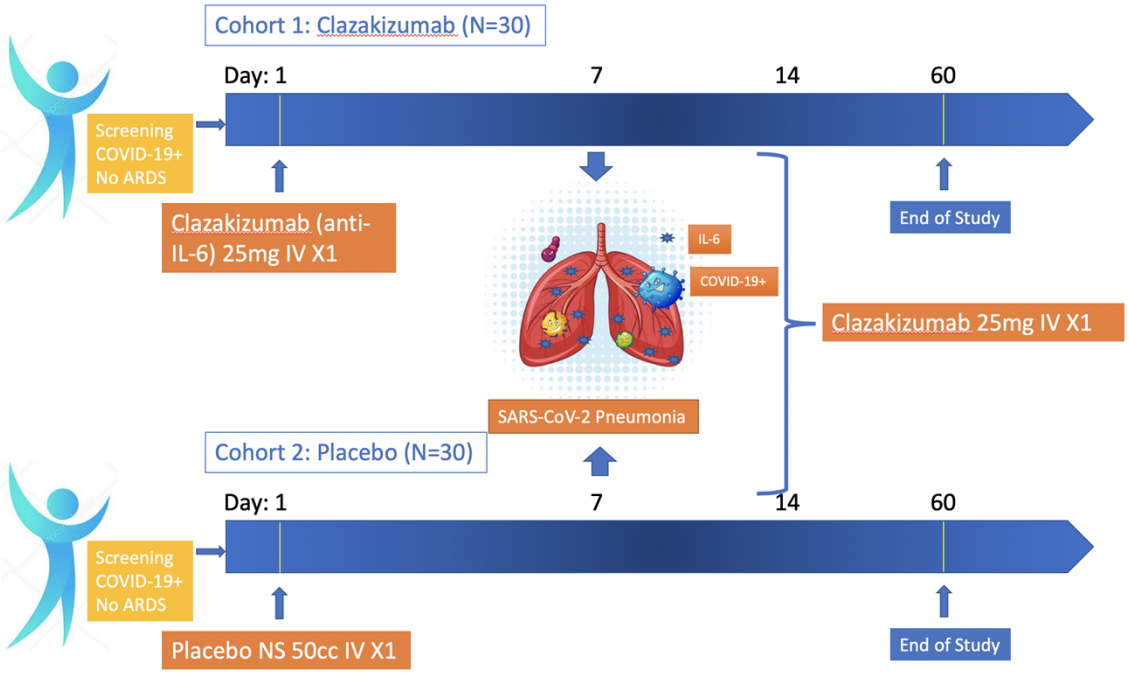

Figure Legend: ARDS = acute respiratory distress syndrome; NS = normal saline; IV = intravenous; mg = milligram; IL-6 = interleukin 6; N = number

How long will you be in the study?
The total time from the first dose of clazakizumab or placebo will be 60 days.

3. WHAT ARE THE POSSIBLE RISKS?

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as an Appendix. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures.

Unknown Risks
There may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be serious, long-lasting, permanent, and/or fatal.

The Frequency of the following side effects is defined as Very Common (10% or greater)

- **Infections (Very Common, 20%):** serious bacterial infections such as tuberculosis, pneumonia and pelvic abscess (a bump-like collection of pus appearing within or just below the surface of the skin) have been seen in the clinical research studies with clazakizumab. There may also be an increased risk with viral and fungal infections. Tell your study doctor if you feel unwell, have flu-like symptoms, fever, muscle aches, weakness and tiredness or severe coughs. You will be monitored very closely for infections during the study.
- **Liver Function Test Abnormalities (Elevated Liver Enzymes and Hepatic Events)**

- **Very Common, Alanine Aminotransferase (liver function test) Increased 14%:** Mild to moderate increases in transaminases (liver enzymes - factors that tell how your liver is functioning) and bilirubin (a level that tells how healthy your liver is) have been seen in blood tests. These abnormal blood test results did not result in any ill-health and resolved without treatment. Tell your study doctor if you notice yellowing of the skin and whites of your eyes; tenderness or swelling in the upper right area of your stomach and fever; dark urine; light-colored, bloody or black bowel movements; vomiting, diarrhea; loss of appetite; unexplained weight change; or tiredness or weakness.

The Frequency of the following side effects is defined as Common (1% or greater, but less than 10%)

- **Blood Abnormalities (Common):** There have been changes to blood cells that help people fight infections (neutrophils) or clot blood (platelets). These blood test results were mild and did not result in any ill-health and resolved without treatment. Your body may not make enough of the blood cells that help fight infections or help stop bleeding. Symptoms include a fever that does not go away, bruising or bleeding very easily, or looking very pale. Tell your study doctor if you notice any of these symptoms or signs.
- **Cholesterol and Triglycerides Abnormalities (Elevated Lipids) (Common):** Increases in total cholesterol and triglycerides were seen in blood tests. These blood test results were mild and did not result in any ill-health and resolved without treatment.
- **Immunogenicity (Common):** This is the development of antibodies that may block the effects of clazakizumab, which could lead to reduced effectiveness or other side effects.

The Frequency of the following side effects is defined as Uncommon (0.1% or greater, but less than 1%)

- **Gastrointestinal Perforations (Uncommon):** This is when a hole forms all the way through the stomach, large bowel, or small intestine. If you have any pain or discomfort in your abdomen, or blood in your stools during the study, please tell your study doctor right away. If you have any inflammatory bowel disease such as Crohn's disease, Ulcerative Colitis, Diverticular Disease or Diverticulitis, you are not allowed to take part in this study.
- **Malignancies (Uncommon):** These are cancers where abnormal cells divide uncontrollably and damage body tissue. There have been cancers considered possibly related to clazakizumab reported in 4 subjects: breast cancer, squamous cell carcinoma of the skin, invasive ductal breast carcinoma and gastric cancer.
- **Hypersensitivity or Anaphylaxis (Uncommon):** Serious allergic reactions have been seen with other antibody drugs that block IL-6. In clinical research studies with clazakizumab, only minor allergic reactions (e.g., skin rash) have been seen.

The Frequency of the following side effects is defined as rare but serious (0.01% or greater but less than 0.1%)

- **Demyelinating Disorders (Rare):** These are conditions that cause damage to your nerves. One case of a demyelinating side effect possibly related to clazakizumab has been seen in the clinical research studies with clazakizumab.

- **Infusion (Allergic) Reactions:** No infusion reactions have been seen with clazakizumab when it is given into the blood directly.
- **Autoimmunity:** Certain autoimmune disorders (e.g., autoimmune hepatitis, lupus-like syndrome) have been seen with the use of some antibody drugs for the treatment of rheumatoid arthritis. No autoimmune disorders were seen in clazakizumab clinical research studies.

Other more common side effects of clazakizumab include the following:

- Injection site reactions (24%)
- Abnormal LFTs (increased alanine aminotransferase (14%), aspartate aminotransferase, gamma-glutamyl transferase, and bilirubin)
- Hypercholesterolemia (increase in cholesterol) and dyslipidemia (abnormal lipid levels)
- Decrease in neutrophil (immune-fighting white blood cell) counts
- Leukopenia (reduction of white blood cells in the blood)
- Upper respiratory tract infections (e.g., colds and sore throats)
- Bronchitis
- Urinary tract infections
- Decrease in platelets counts
- Increased triglycerides
- Nausea
- Cellulitis (bacterial skin infection)
- Herpes zoster infection
- Asthenia (weakness or lack of energy)
- Rash
- Oral herpes infection
- Dizziness

Reproductive and Lactation Risks

Taking part in this research study can affect an unborn baby. Therefore, you should not become pregnant or father a baby while on this study. If you or your partner is capable of becoming pregnant you will need to use birth control. Check with the researcher about approved birth control methods to use while participating in this study.

Women should not breastfeed a baby while on this study.

Unknown Risks to the Developing Embryo or Fetus (an unborn baby)
If you are pregnant, or become pregnant during participation in this research, the study drug might involve risks to an embryo or fetus, which are currently unknown. It is important that you contact the researcher immediately if you believe you might be pregnant.

Collection of Pregnancy Outcomes
If you become pregnant during the study, we will collect information on the outcome of your pregnancy including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, abnormalities, or complications, and the health status of your child. By signing this consent, you are agreeing to have this information about you and your child collected from your medical records in the rare case that you become pregnant during your participation in this

research study, however, you are always free to withdraw your consent to participate in any research procedure.

Participation in a double-blind study means that you may not be able to participate in other, similar trials since unblinding would generally only occur for emergent, life-threatening situations. We might not be able to tell you if you received the study drug or placebo in a situation where you would like to qualify for another research study. Because you may not know the study group to which you were assigned, in the future should you wish to participate in a different study that requires knowing what drug you received in this study, you may not be eligible to participate in the different study.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

If you agree to take part in this research study, there may or may not be direct medical benefit to you. Possible benefits of treatment of COVID-19 with clazakizumab include improvement in lung function (ability to breathe with less assistance or without assistance) and reduction of fevers. However, no benefit is guaranteed. It is possible that your condition may remain unchanged or even get worse.

We hope the information learned from this research study will benefit other individuals with COVID-19 infection in the future by helping us to learn if clazakizumab is better than placebo to inhibit or block these inflammatory processes in order to try to limit the damage COVID-19 causes to the lungs.

5. WILL I BE INFORMED OF RESEARCH RESULTS?

All the research tests done in this study follow standard clinical procedures and are performed in certified clinical labs. These test results may be shared with you and may be placed in your Cedars-Sinai medical record.

6. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:

- The study is stopped or suspended;
- Funding for the study is reduced, stopped or withdrawn;
- If it is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures.
- The study maybe be stopped or suspended if a patient's condition worsens while in treatment, possibly indicating lack of efficacy of clazakizumab.

You may choose (or you may be required) to withdraw from certain parts of the study but invited to continue with other parts. For example, you might stop taking a study drug, but continue with follow-up visits or allow us to continue to collect data from your medical records. Separate written consent will be requested if your continued participation will involve procedures not described in this consent form.

7. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary, so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

If you decide not to take part in this study, you have other choices. For example:

- you may choose to be treated following the usual clinical approach
- you may choose to take part in a different study at CSMC or elsewhere, if one is available
- you could decide not to be treated.

There is no FDA-approved treatment for COVID-19. There may be other off-label or investigational drugs being tried to treat COVID-19. You should discuss these options with your treating doctor.

The researcher will discuss these options and their risks and benefits with you.

8. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research oversight, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

Attached to this consent form is an "Authorization Form" that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

We might share your information and/or research samples collected in this study with other researchers at Cedars-Sinai, other academic institutions, or third party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

9. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

Contact your study doctor at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your study doctor of your situation at the phone number listed on page 1 of this consent form.

Who pays for my research related illness or injury?

Cedars-Sinai has no plans to pay for costs associated with the treatment of research-related injury or illness. We will make every effort to seek reimbursement from your health plan. However, you will be responsible for any deductibles and co-payments required under your health plan and for any claims ultimately denied by your health plan. Financial assistance may be available under Cedars-Sinai's Charity Care Policy and Procedure. If you feel that you have had a research-related injury and need financial assistance, please contact the IRB Office at 310-423-3783. You do not waive any of your legal rights by signing this form.

FINANCIAL CONSIDERATIONS

Costs of Participation

Please review the attached Appendix flowchart for a listing of items, drugs and services that will be billed to you and/or your insurance and those that will be covered by the study sponsor.

Only items, drugs and services that are reasonable and necessary for your medical care throughout the study will be billed to your insurance. You remain responsible for all deductibles, co-pays, and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. You should check with your health benefit plan if you have questions or concerns about your insurance coverage.

Compensation for Participating

You will not be paid for taking part in this research study.

Financial Interest in the Research

A significant financial interest is a situation in which financial considerations have the potential to influence a person's professional judgment. This study has been designed to minimize the impact of the investigator's financial interest. You are encouraged to ask the investigator to explain how the financial interest disclosed below will be managed.

Dr. Jordan receives payment from and has an ownership interest in Vitaeris, the company providing the investigational drug for this study. He receives payment for providing professional consulting services and medical expertise in kidney transplant and has also received a research grant for conducting a study like this clinical trial.

The PI and institution have no other potential financial conflict of interest with respect to this study.

10. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact one of the investigators listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP) Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

11. CONSENT PROVISIONS

If you sign this form below, it means that:

(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights (other than the postponement of your access to certain health information as described in this informed consent form);
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights", if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and the Experimental Subject's Bill of Rights.

SIGNATURE PAGE
Consent Form for Research and
Authorization for Use and Disclosure of Identifiable Health Information (Research)

SIGNATURE BY THE PARTICIPANT OR LEGAL REPRESENTATIVE:

Name of Participant (Print)	Signature of Participant	Date of Signature

If participant is unable to sign the form, please state the reason below:

_____

Signature of Legal Representative	Relationship to the Participant	Date of Signature

Authorization for Use and Disclosure of Identifiable Health Information (Research)): *I hereby agree that my identifiable health information may be used and/or disclosed in accordance with this "Authorization for Use and Disclosure of Identifiable Health Information (Research)" form attached as Appendix to this form.*

Name of Participant (Print)	Signature	Date Signed

SIGNATURE BY THE INVESTIGATOR: *I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.*

Name of Investigator (Print)	Signature	Date Signed

SIGNATURE BY THE INTERPRETER/WITNESS

(Signature of an interpreter is only required when a non-English speaking subject is consented with the assistance of an interpreter. The interpreter may be any person who is conversant in both English and the language of the Non-English speaking subject, such as the interpreter (the certified hospital interpreter), study staff, a family member, or other person. The interpreter signs the consent forms to confirm that the oral interpretation occurred.

Signature of a witness is required when an English-speaking subjects who has been determined to have capacity to consent is unable to read or physically sign the consent form, but choses to indicate via a "mark" or verbally that he/she agrees to participate. The witness signs the consent form to confirm that an oral consent process occurred and that the individual verbally consented to participate in the research.

Name of Witness (Print)	Signature	Date Signed

CEDARS-SINAI MEDICAL CENTER

APPENDIX: EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

CEDARS-SINAI MEDICAL CENTER

AUTHORIZATION FOR USE AND DISCLOSURE OF IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH

- **USE AND DISCLOSURE OF HEALTH INFORMATION**

If you agree to this Authorization, you give permission to the research team at Cedars-Sinai Medical Center ("CSMC") to use or disclose your identifiable health information ("private information") for the research study titled "A Phase II Trial to Evaluate the Safety and Tolerability of Clazakizumab® (Anti-IL-6 monoclonal) compared to placebo for the treatment of COVID-19 infection" which is described in the Consent Form for Research ("Consent Form") to which this Authorization is attached. In particular, you authorize the research team acting under the direction of the Principal Investigator to review your medical records and collect your private information from the following sources:

☒ Laboratory tests
☒ Pathology reports
☒ Imaging reports (e.g., x-rays or scans)
☐ Photographs or videos of your image
☒ Doctor/clinic records
☒ Hospital/medical records
☐ Mental health records
☐ Billing records
☒ Other tests or other types of medical information: Demographics and diagnosis

- **WHO WILL HAVE ACCESS TO YOUR PRIVATE INFORMATION?**

Your private information will be used by and/or shared with the CSMC investigators listed in Section A of the Consent Form and their research staff.

In addition to the research team, if applicable, the following parties may receive your private information and inspect your records:

- The reviewing Institutional Review Boards and CSMC offices with authority to oversee research compliance.
- U.S. government agencies, such as the Food and Drug Administration and the Department of Health and Human Services.
- Researchers at other organizations who are participating in this research study.
- The Study Sponsor and organization providing the investigational product and its business partners, for matters related to research study oversight, data analysis and use of research results in product development.

- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, with the Sponsor and/or the FDA.

CSMC is required by law to protect your private information. However, the recipients described above may re-disclose (or share) your information with other parties unless such sharing is prohibited by law.

- **WHEN WILL MY AUTHORIZATION EXPIRE?**

By signing this document, you authorize the use and sharing of your private information until the end of the research study.

- **REVOKING AUTHORIZATION**

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the research team may still use or disclose private information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to the Principal Investigator of the research study. The mailing address is: **8900 Beverly Blvd, Los Angeles, CA 90048**.

- **NOTICE OF RIGHTS AND OTHER INFORMATION**

You do not have to agree to this Authorization, but if you do not agree, you may not participate in the research study. CSMC may not condition (withhold or refuse) treating you on whether you agree to this Authorization.

If you agree to this Authorization, please sign on the appropriate signature line below. You will receive a copy of this Authorization

APPENDIX A: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks

The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.

Study Procedure	Related Risks
Blood draw: A needle is placed in the vein in your arm to draw blood	Blood drawing may cause some pain and has a small risk of bleeding, bruising, or infection at the puncture site. There is also a small risk of fainting.
Infusion Procedure: Infusion is the administration of drugs directly into your bloodstream using intravenous (IV) lines. The risks associated with IV lines are described separately below.	Occasionally, people have allergic reactions (including life-threatening reactions) when taking any medication. Symptoms of any allergic reaction can include a rash, hives, itching, and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face, and rarely death. If you experience any difficulty breathing, closing of the throat, swelling of the lips, tongue or face, or hives, you should stop taking your study drug and immediately seek emergency medical attention. In general, allergic reactions to medicines are more likely to occur in people who have allergies to other drugs, foods, or things in the environment, such as dust or grass. If you have allergies to other medicines, foods, or other things in the environment, or if you have asthma, you should let your researcher know.
Intravenous (IV) lines: You will receive the study drug or other medications or contrast agent through an intravenous (IV) line. An IV line is a small tube that is attached to a catheter and inserted by needle into a vein usually in your hand or arm. Qualified medical professionals will place IV lines for use in this study.	IV lines are usually safe and well tolerated and complications are rare, but can include phlebitis (swelling of the vein) and infection. The IV may come out accidentally or blood may leak around the line. If the IV is not in the vein, medication or fluid can enter the surrounding soft tissues, and can be associated with swelling, discomfort, bruising and irritation. Rarely, a clot can develop in the IV line itself. If this happens, the staff may remove the old IV line and start a new IV line. There is also a small risk of feeling lightheaded and fainting.
Physical Exam: Includes height, weight, vital signs (heart rate and blood pressure)	There are no physical risks associated with these procedures.
Concomitant Medications: You will be asked about your previous and current medications that you take.	There are no physical risks associated with these procedures.

Medical History Review: You will be asked about your medical and surgical history with attention to the COVID19 infection and your lung function	There are no physical risks associated with this procedure.
Demographic Information: You will be asked about your age, gender, race, ethnicity	There are no physical risks associated with these procedures.

Study No.: CLAZACOVID19		**Short Title: Clazakizumab for Covid 19**			**Status: New**		
	Treatment						
	Screening 1@1Days	**Treatment 1,3,7,14,28,60@60Days**					
Re-labelled visits	Screening						Day 60 (EOS)
	D1 [#2]	D1 [#2]	D3	D7 [#3]	D14 [#3]	D28	D60
Medical History	S				S		
Complete Physical Exam	S	S			S		
Randomization		R					
Data collection: Hemodynamic and respiratory parameters	R	R	R		R		
Informed Consent		R					
Inclusion/Exclusion criteria review	R						
TB testing [Quantiferon TB Gold] [#1]	RB						
Blood test: IL-6, CRP, Ferritin, D-dimer, Troponin, Procalcitonin, LDH, BNP		S		S			
Blood test: CBC with differential		RB		RB			
Blood test: Treg profile		R	R				
Review Chest X-Ray (collected by SOC[standard of care])					R		
Concomitant Medication	R				R		
Clazakizumab/Placebo infusion		RB					
Clazakizumab/Placebo		R					
Open Label Clazakizumab [#4]			R				
Open Label Clazakizumab infusion			RB				

	Screening 1@1Days	**Treatment 1,3,7,14,28,60@60Days**					
Re-labelled visits	Screening						Day 60 (EOS)
	D1 [#2]	D1 [#2]	D3	D7 [#3]	D14 [#3]	D28	D60
Adverse Event Monitoring		R			R		R
Assess blood tests: CMP, COVID-19 panel labs collected by SOC (standard of care)			R		R		
Assess Survival Status						R	R
Assess use and duration of proning (prone position to improve respiratory flow)					R		
Pregnancy test for WOCBP (ages 18--55) [#6]	R						
Assess new infections					R		
Assess investigational antivirals administered [#5}							R
Legend:							
R = Research item/procedure done only for research purposes and covered by the study							
S = Standard of care item/procedure that is part of regular care and billed to the patient/insurance							
RB = Research item/procedure that is related to use of the study device or administration and monitoring of study drug, but billed to the patient/insurance							
Calendar Foot Notes							
#1. At or within one month prior to screening date.							
#2. May be combined (Screening Day and Day 1). Any duplicate items will be collected once. Blood test: comprehensive metabolic panel [CMP] performed per standard of care will be assessed.							
#3. Or at discharge, whichever occurs first.							
#4. Patients who decompensate before Day 14 can receive open label Clazakizumab							
#5. during hospitalization only; up to study day 60							
#6. At or within one week of screening							