ADULT INFORMED CONSENT

COH Protocol # 20291 (Phase 1)
TITLE: A Phase 1/2 Trial of Leflunomide for the Treatment of Severe COVID-19 in Patients with a Concurrent Malignancy
Version date: 06/25/20

PRINCIPAL INVESTIGATOR: Sanjeet Dadwal, MD

24-HOUR TELEPHONE NUMBER: (626) 256-HOPE (4673) ext. 85200
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EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study, also known as an experiment or clinical trial. As a research participant, you have the following rights:

1. To be told what the research study is trying to find out.
2. To be told what will happen to you and whether any of the procedures to be used are different from what would be used in standard practice.
3. To be told about the discomforts, side effects and risks of the things that will happen to you as part of the research study.
4. To be told if you can expect any benefit from participating in the research study.
5. To be told of the other choices you have and how they may be better or worse than being in the research study.
6. To be told what medical treatment is available if any complications arise.
7. To be allowed to ask any questions concerning the research study, both before agreeing to be in the study and during the course of the study.
8. To refuse to participate in the research study or to change your mind about participation after the study is started. To be informed that this decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated research study consent form.
10. To be free of pressure when considering whether you wish to agree to be in the research study.

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KEY INFORMATION
You are invited to participate in a research study. The purpose of this research study is to estimate the safety and effectiveness of a drug called leflunomide against severe COVID-19. The information we learn by doing this research study might eventually contribute to leflunomide being used as a treatment for this disease.

Participants will undergo screening tests to see if they are eligible for the study. Eligible patients will be given leflunomide as an addition to the currently standard methods (including other drugs and patient care) to treat COVID-19.

The major risks associated with this study include liver toxicity, abdominal pain, diarrhea, nausea, vomiting, ulcers in the mouth, upper respiratory tract infections, loss of hair, rash, headache, and dizziness.

You do not have to join this research study. You can choose to receive standard methods to approach COVID-19 instead of participating on this study. If you are interested in learning more about this study, please continue to read below.

INTRODUCTION

You are invited to take part in a clinical trial, a type of research study, because you have COVID-19 and also a past or present cancer. We hope to learn whether there is evidence that leflunomide may be effective against COVID-19 and that it is safe in this setting. This research study is looking at leflunomide as a possible future treatment for this diagnosis.

This research study is sponsored by City of Hope.

It is expected that about 9-12 people will take part in this research study.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future. Please take as much time as you need to read the consent form. If you find any of the language difficult to understand, please ask questions. If you decide to participate, you will be asked to sign this form. We will give you a copy so

that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This is a Phase I/II clinical trial. You are being asked to participate in the Phase I portion of the study. A Phase I clinical trial tests the safety of an investigational (experimental) intervention and tries to define the appropriate dose of the investigational intervention to use for further studies. "Investigational" means that the intervention is being studied.

The FDA (the U.S. Food and Drug Administration) has not approved leflunomide for your specific disease, but it has been approved for other uses.

The names of the study interventions involved in this study are:

- Administration of study drug: leflunomide
- Administration of cholestyramine after treatment: Cholestyramine helps remove leflunomide from the body
- Collection of blood to monitor drug levels and to see how leflunomide affects the immune system

In this research study, we are expecting to learn whether leflunomide is safe for patients with COVID-19, and whether it is potentially effective against the disease.

- Leflunomide has been used since the 1990s as a treatment for rheumatoid arthritis, so we anticipate that the drug will be safe.
- Experiments done with human cells that were given SARS-CoV-2, the virus causing COVID-19, showed that leflunomide was able to reduce the ability of the virus to make copies of itself.
- The coronavirus uses RNA, a very long molecule that contains genetic information that is like a blueprint for making more copies of itself. Leflunomide inhibits the formation of RNA.

B. WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:

Before the research starts (screening):

After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history,** which includes questions about your health, current medications, and any allergies.

- **Blood tests** to check your blood counts and organ function (about 3 teaspoons will be drawn from a vein in your arm)
- **An oxygen test** to determine how much oxygen is in your blood. This is measured by placing a sensor over your fingertip.
- **Pregnancy test** if you are a woman of childbearing potential by drawing about ½ teaspoon of blood usually from a vein in your arm, or by a urine test
- **Tuberculosis Test:** skin test, blood test, and/or chest x-ray. When required by law, any positive results will be shared with a health authority (e.g., the State Department of Health)

If these tests show that you are eligible to participate in the research study, you will begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Additional research procedures to be performed at the time of screening but not required to determine eligibility:

- **Blood tests** for research purposes to see how leflunomide affects the immune system (about 2 teaspoons will be drawn from a vein in your arm)
- **Pharmacokinetic (PK) blood samples:** PK blood samples to monitor how your body absorbs and breaks down the study drug. Each blood sample will be approximately 1 teaspoon.

Hospitalization: Because of the severity of your disease, we want to carefully monitor your condition. You will be in the hospital for at least the first 7 days of your treatment. After 7 days, you will leave the hospital when you are healthy enough to return home.

Study Procedures:

If you are eligible to participate in this research study, the following tests and procedures will occur. A chart summarizing the timing of these tests and procedures is also provided below. Some tests and procedures may be part of your standard of care.

- **Oral Study Drug(s)** Leflunomide lasts 14 days, during which time you will be taking the study drug by mouth once per day.
- **Cholestyramine** is not an experimental agent but is required to help your body get rid of leflunomide when you have finished taking part in this study.
- **Other Medications**: While you are receiving study treatment, you should not take other medications without first discussing them with the study doctor. These include drugs that affect how the body processes leflunomide, specifically known as CYP1A2 inducers (like rifampicin) and CYP2C8 inhibitors (like clopidogrel). Vitamin K antagonists (like warfarin) should also be monitored, because cholestyramine may also deplete vitamin K supply. Their use should be monitored by your doctor. The reason your doctor should review other medications is that they may give you harmful side effects when combined with this treatment.

- **Clinical Exams:** During this visit you will have a physical exam and you will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.
- **Blood tests**:
    - For research purposes to check on leflunomide levels in the blood, and to study the effects of leflunomide on the immune system (about 2 teaspoons of blood will be drawn each time)
- **Nasopharyngeal swabs,** a swab taken inside your nose, to measure levels of SARS-CoV-2. If you will be on a ventilator a swab of your windpipe will be done if safe and feasible.
- **Allowed Medications**: Other medications and other interventions (for example, remdesivir, convalescent plasma, and tocilizumab) are allowed. Your doctor may decide to give one or more of these interventions as part of your standard of care or supportive care.
- **Medications to be monitored**: CYP1A2 inducers, CYP2C8 inhibitors and vitamin K antagonists
- **Optional Research Tests:** At the end of this consent form, you will be asked to decide if we can keep your samples and store them for future testing.

Research Study Calendar:

	Screening	Treatment + Monitoring (Days 1-28)	End of Treatment					
			D 29-39	D 40	D 42	D 56	D 70	D 90
Medical history	X							
Physical exam and vital signs	X	X[1]						
Pregnancy test	X							
Oxygen test	X							
Hospitalization		Days 1-7[2]						
Blood tests	X	X[1]	X[3]	X[3]		X		X
Samples to measure viral load		Days 2-14, every other day						
Assessments of disease status	X	X						
Blood tests for research	X	Day 1-14[1] Days 21, 28						
Leflunomide		Days 1-14 Daily						
Cholestyramine			X					
Side effect evaluation	X	X			X	X	X	X

1. This is will be done twice a week if you have left the hospital.
2. After 7 days, you will leave the hospital when you are healthy enough to do so.
3. A blood test will be performed weekly while you are taking cholestyramine. Blood tests will also be performed at the end of the course of cholestyramine and at least 14 days after that, in order to make sure that leflunomide has been cleared from your body and that the cholestyramine has not caused any bleeding abnormalities.

Planned Follow-up: After you complete the 28-day treatment and monitoring period, you will be followed up to 90 days after start of treatment. During planned follow-up, you will make the following visits:

- **Safety Follow-up:** Blood tests will also be performed at the end of the course of cholestyramine and at least 14 days after that, in order to make sure that leflunomide has been cleared from your body and that the cholestyramine has not caused any bleeding abnormalities. You will be asked to visit your doctor on days 56, and 90 for blood tests to check on your side effects. We will also check on your side effects on days 42 and 70; this evaluation may be performed as a tele-health visit.

C. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for about 90 days.

D. WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There are risks to taking part in any research study. One risk is that you may get a study drug or study dose of a drug that does not add benefit to standard of care or that makes your condition or disease worse. Another risk is that there may be side effects.

All treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drug to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. You will be monitored closely for any severe, life-threatening side effects listed below. Some of these side effects may be permanent. Appropriate medical care will be provided, if necessary, including additional treatment, hospitalization and/or surgery.

Possible risks and discomforts you could experience during this study include:

Risks Associated with Leflunomide:

Most Common Side Effects (More than 10 out of 100 research participants)

- Diarrhea or loose/frequent bowel movements
- Respiratory infection (cough)
- Headache

- Nerve pain and/or numbness, tingling in hands, feet, legs
- Rash
- Itching and dry skin
- Hair loss (alopecia)
- Hair discoloration
- Loss of appetite, changes in taste, weight loss
- Leg cramps

Common Side Effects (10 out of 100 research participants)

- High blood pressure, which could be fatal. If this occurs, medications may be prescribed to manage it.

Less Common Side Effects (1 to 3 out of 100 research participants)

- Lowered red cells or anemia which may make you feel tired
- Chest pain
- Irregular heart beat
- Diabetes (high level of sugar glucose in the blood)
- Blurred vision, cataract, inflammation of the eye lids (conjunctivitis) (painful red eyes), eye disorder
- Abdominal pain, upset stomach, nausea, vomiting
- Mouth Sores
- Loss of appetite (anorexia)
- Constipation
- Painful difficulty swallowing
- Belching/bloating
- Inflammation of the lining in the stomach (for example, heartburn, nausea)
- Irritation, redness and swelling of the gums, bleeding, yeast infection of the mouth, inflammation of the back of the throat, infection of the salivary gland, mouth sores, tooth disorder (for example, tooth infection)
- Elevated liver enzymes. These are enzymes located in the liver that help detoxify the blood and provide nutrients for the body. Excessive release into the bloodstream is a sign of a damaged liver.
- Mild rash
- Infections (cold/flu like symptoms, runny nose, inflammation of the bronchial tubes and throat, pneumonia, and urinary tract, yeast, fever blisters, rash, skin and fungal), including infection of the blood that may be fatal
- Bone and muscle pain, muscle cramps
- Difficulty sleeping
- Dry mouth

- Anxiety
- Night sweats
- Dizziness
- Difficulty urinating or increased urge
- Irregular menstrual cycles
- Asthma, lung disorders
- Urinary tract disorders or infections
- Acne
- Nail or skin discoloration
- Swelling
- Hernia (this occurs when an organ or fat squeezes into a weak spot or tear in the muscle wall)
- Neck and pelvic pain
- Feeling of unease, depression

Rare but Serious Side Effects (less than 1 out of 100 research participants)

- Condition in which the number of white blood cells called neutrophils is abnormally low (neutropenia). This increases your risk of infection, which may be serious or life-threatening
- Lowered white blood cells called lymphocytes that may lead to an increase in infection
- Lowered red blood cells, white blood cells and platelets at the same time that may lead to an increase in infection, an increase in bruising or bleeding and/or may cause you to feel tired.
- Inflammation of the pancreas (Pancreatitis)
- Liver disease, inflammation of the liver, liver failure, which may be life-threatening. (Note: liver failure is sometimes fatal.)
- Urinary tract infections
- Serious allergic reactions, itchy, rash, throat swelling, that may be fatal
- Fungal infections including infection of the bloodstream, that may be fatal (especially fungal pneumonia, tuberculosis, aspergillosis)
- Secondary cancers
- Lung disease (sometimes fatal)
- Lung inflammation, possibly difficulty breathing
- Lung damage which can cause shortness of breath
- Skins disorders such as Stevens-Johnson syndrome (flu like symptoms, painful rash and blisters), can be life threatening
- Jaundice (yellowing of the skin and the whites of the eyes)
- Hives

<u>Risks Associated with Cholestyramine:</u>

Most Common Side Effects (More than 10 out of 100 research participants)

- Constipation
- Heartburn or indigestion

Less Common Side Effects (1 out of 50-100 research participants)

- Abdominal pain
- Loss of appetite
- Nausea
- Vomiting
- Diarrhea,
- Belching
- Bloating
- Dizziness
- Headache

Less Likely (less than 1 out of 100 research participants)

- Anemia, blood disorder
- Ringing in the ears
- Dizziness, feeling of losing balance
- Inflammation of the eye
- Formation of a hole in the small and/or large bowel particularly in people with preexisting bowel problems. This side effect may be serious and life-threatening.
- Hiccups or a sour taste in your mouth
- Itching or irritation around your rectal area
- Muscle or joint pain
- Inflammation of the pancreas
- Tooth enamel damage (dental erosion), dental bleeding, dental cavities, dental discoloration
- Liver disease, inflammation of the liver, liver failure, may require additional medication, and hospitalization, can be fatal
- Allergic immune reactions
- Acidic body fluids, which means that your body fluids are more acidic than normal. One effect is an imbalance of chemicals in your bloodstream.
- Back, body, muscle pain, nerve pain
- Loss of bone strength, increased risk of fracture associated with vitamin D deficiency
- Anxiety
- Dizziness
- Tiredness, drowsy
- Headache
- Asthma, difficulty breathing and wheezing associated with an allergic reaction
- Urinary infections, blood in urine, discoloration, smell
- Skin disorders, itching rash, hives

- Swelling, swelling of the lymph nodes
- Increased sex drive
- Weight loss or weight gain

Additionally, cholestyramine, by potentially interfering with the absorption of other substances from the digestive system, may lead to vitamin deficiencies (vitamin A, D, E, K). Of note, a deficiency in vitamin K may cause bleeding, as vitamin K helps thicken blood.

Since the effect of the study drug taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

Risks Associated with Blood Draw

Risks of blood draws include mild pain or discomfort, bruising and swelling around the puncture site, dizziness or fainting, or infection (rare).

Incidental Findings:

It is possible the research procedures could find a medical problem unrelated to the purpose of this study that you did not know about before. If during the research procedures we learn information that may be important for you to know about, such as the possibility of a previously unknown medical condition, we will tell you. You may authorize the release and communication of the findings to your personal doctor. These findings may require additional testing or treatment. You will be responsible for the cost of any additional tests or related treatment.

Reproductive Risks:

We do not know whether this drug might hurt an unborn child. While participating in this research study, you should not become pregnant or father a baby, and should not nurse a baby. We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

In the event that your partner becomes pregnant, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens. The study sponsor may want to collect data on your partner's pregnancy.

If you are pregnant or nursing a baby and do not want to stop, you cannot take part in this study. If you are a woman who can become pregnant, a urine pregnancy test will be obtained before treatment is started. If you are sexually active and capable of bearing or fathering a child, both you and your partner must agree to use a medically effective form of birth control while you are on this study. The investigational drug(s) may involve risks to you (or to the embryo or fetus, if you or your partner become pregnant), which is currently unforeseeable.

You must use birth control while on this study. Acceptable medically effective forms of birth control are:

- Abstinence,
- Surgical sterilization (tubal ligation or hysterectomy for women, vasectomy for men),
- Double-barrier methods (i.e. condoms, diaphragm, cervical cap, or sponge used with spermicidal gel or foam),
- Intrauterine device (IUD) (i.e. Progestin, Copper),Hormonal Contraceptives (Birth control patches, implants, pills, rings, or injections)

Other Risks:
Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

Risks associated with Breach of Confidentiality*:*
There is a small risk that people who are not connected with this study will learn your identity or your personal information.

E. WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. HOW WILL YOUR INFORMATION BE KEPT CONFIDENTIAL?

Any information learned from this study in which you might be identified will be confidential and disclosed only with your permission. Every effort will be made to keep any information collected about you confidential. However, it is impossible to guarantee that information about you will not be mistakenly released. If, despite our best efforts, identifying information about you is released, it could negatively impact you or your family members. This risk is small.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor, City of Hope
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- Regulatory agencies such as the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the National Cancer Institute (NCI) in the U.S., and similar ones if other countries are involved in the study as required by law.

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.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The Certificate protects against the release of information, documents or biospecimens that may identify you that was collected during the period the Certificate is in effect to individuals not connected with the research. For example, the researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you choose to voluntarily disclose the protected information under certain circumstances (for example, if you request the release of information in writing), the Certificate does not protect against that voluntary disclosure. Additionally, the Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document, for other scientific research, as allowed by federal regulations protecting research subjects, or for your medical treatment.

Future Use of Research Information and Specimens

In the future, the information or specimens that have been collected for this study might/will be de-identified, which means any information that could be used to identify you will be removed from the information or specimens. The de-identified information or specimens may be used for future research studies or shared with other researchers. You will not be informed of or asked to consent to these future research activities.

G. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS RESEARCH STUDY?

There is no guarantee that you will receive any benefits from this study. The possible benefit of the study drug in the treatment of COVID-19 is not known. If you decide to participate in this study, your health will be monitored very closely. By being in this study, you will give doctors more information about how well the study drug works. It may help doctors understand your condition better and may help future patients with this medical condition.

H. WHAT OTHER OPTIONS ARE THERE?

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

- You may choose to have the usual approach for your disease,
- You may choose to take part in a different study, if one is available, or
- You may choose not to be treated for your disease, but you may want to receive comfort care to relieve symptoms.

I. ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

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

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.

Leflunomide and cholestyramine will be provided to you at no cost while you take part in the study. It is possible that leflunomide and cholestyramine may not continue to be supplied while you are on the study. If this occurs, the research doctor will talk to you about your options.

Most of the tests, procedures, and/or drugs provided to you as part of this study are routinely used to treat your illness. You would receive these tests, procedures, and/or drugs even if you were not participating in this study. You or your health plan/insurance company will need to pay for this routine care. You will also be responsible for any co-payments or deductibles required by your health plan/insurance company. Some health plans/insurance companies will not pay the costs associated with these tests, procedures, and/or drugs because you are in a research study. If your health plan/insurance company will not pay these costs, you will have additional expenses from being in this study, such as the costs associated with treating side effects.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- City of Hope Financial Support Services: 626-256-HOPE (4673), extension: 80258.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF YOU GET INJURED AS A RESULT OF THIS STUDY?

If you think you have been hurt by taking part in this study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent

form. City of Hope will offer you the care needed to treat injuries directly resulting from taking part in this research. This care will be billed to you or your insurance company. You will be responsible for deductible and co-payments, or any costs not paid by your insurer. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

L. WHAT ARE YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE? Your participation in this research study is voluntary. You are free to withdraw your consent for participation in this study without any loss of benefits, penalty, or interference with any future treatment at City of Hope.

You can decide to stop at any time and you may still be treated at your hospital or clinic. Tell your study doctor if you are thinking about stopping or decide to stop. You should talk to the doctor about leaving the study before you decide so that he/she can find out if you are having any side effects from study treatment. Another reason to tell your doctor that you are thinking about stopping is so that he/she can talk to you about any other treatments that could be helpful to you.

If you decide to stop being in this study, you will still be asked to come back to the hospital or clinic for the end of treatment tests described above. You may also be asked to take part in the follow-up phone calls and/or visits. This information is important to make sure that there are no lasting side effects from the study treatment and to see if your condition got better, stayed the same, or got worse after treatment.

M. CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons: you do not follow the investigator's or study doctor's instructions, at the discretion of the investigator or the sponsor, or the sponsor closes the study. If this happens, the investigator or study doctor will discuss other options with you.

N. WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

The principal investigator, Dr. Dadwal or a colleague, Dr. _____, responsible for your care or treatment, has offered to and has answered any and all questions regarding your participation in this research study. If you have any further questions or in the event of a research related injury, you can contact Dr. Dadwal at (626) 256-HOPE (4673) ext. 88202 or Dr. _____ at (626) 256-HOPE (4673) ext. _____.

This study has been reviewed and approved by the Institutional Review Board (IRB). If you have any questions regarding your rights as a research participant, you may contact a representative of that Board, from the Office of Human Research Subjects Protection, at (626) 256-HOPE (4673) ext. 62700.

O. ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in. You will make your selection at the end of this section. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with COVID-19 or cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say "no" to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

At the end of the document, circle your choice of "yes" or "no" for each of the following studies.

Optional Collection of Blood and Tissue for Future Research Studies

Researchers are trying to learn more about COVID-19, cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

The researchers ask your permission to store and use your samples and related health information (for example, your response to treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking".

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) Your blood samples, including possibly specimens left over from diagnostic and clinical tests, and some related health information may be stored in the Biorepository (Biobank), along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
2) Qualified researchers can submit a request to use the materials stored in the Biorepository (Biobank). An ethics committee review will be done to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you

3) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
4) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biorepository (Biobank) staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom City of Hope sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part.

Your samples may be helpful to research. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Some of this research may result in new inventions or discoveries that may be of potential commercial value and may be patented and licensed for the development of new products. Donors of blood, tissue and other biological materials do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries. Your decision not to allow storage or future use of your tissue or specimens will not affect your ability to participate in this study.

WHAT IF I CHANGE MY MIND?

If you agree to allow your specimens to be used for future research, you can change your mind later. If you change your mind, please ask for the "Withdrawal of Informed Consent to Continue in Participation in Research Activities" for IRB #20291." Please sign the section of this this withdrawal form named "Biological Specimen Withdrawal of Consent" and send it to the principal investigator of this study at City of Hope. Once City of Hope notifies its specimen bank of this withdrawal of informed consent and the specimen bank processes your signed withdrawal of informed consent, your specimens will not be used in any new research. At that time, any of your existing specimens will be destroyed.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, Sanjeet Dadwal, at (626) 256-HOPE (4673) ext. 88202.

Please circle your answer to show whether or not you would like to take part in each option:

Samples for Future Research Studies:

1. My samples and related information may be kept in a Biorepository (Biobank) for use in future health research.

YES NO

This is the end of the section about optional studies.

P. SIGNATURE SECTION

SIGNATURE FOR CONSENT: By signing this consent form, you are making a decision to participate in this research study. Your signature on this informed consent form indicates that you:

1. Have read and understood the information in this form.
2. Have had the information in this form explained to you.
3. Have had a chance to ask questions and these questions were answered to your satisfaction.
4. Have been informed that you will receive a copy of this signed consent form, which includes the "Experimental Subject's Bill of Rights."

I hereby agree to be a research participant in this research study:

_____ _____ _____

Research Participant's Signature Date Time

(For paper consent only, date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

NOTE: To determine who should sign below, review the guidance document, *Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?*

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

_____

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name

A Phase 1/2 Trial of Leflunomide for the Treatment of Severe COVID-19 in Patients with a Concurrent Malignancy

AUTHORIZATION TO USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION (PHI) FOR PURPOSES OF THIS STUDY:

I. **Purpose of this Authorization**: The information about your health is something that is protected by law and cannot, except for certain purposes, be disclosed (shared) without your permission. As part of this research, you are agreeing to allow City of Hope, its affiliated research doctors, healthcare providers, and physician network to use and share with others your protected health information ("PHI"), as needed for the research. If you agree to participate in the study named above (called the "Study"), you must sign this authorization in addition to the *Study Consent Form*.

II. **The Information About You that is Covered By this Authorization**: PHI refers to information that we maintain about you that identifies you and includes the information contained in your medical record. Your medical record consists of information related to your health and the treatment we provide to you, such as your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures. If you sign this authorization, you are allowing City of Hope and the individuals indicated below to use and share any PHI we maintain about you that is required for your participation in the Study.

III. **Purposes for Uses and Sharing of your PHI; Who Will Use, Share and Receive your PHI**: Your PHI will be used and shared with others for the purpose of doing this research as described in the *Study Consent Form*. Your PHI will also be used to keep the research sponsor informed about this Study, for reporting to those individuals and authorities responsible for overseeing our research activities to make sure that the activities are properly conducted, and to report to regulatory agencies as required by the Study.

The people authorized to use and share your PHI for purposes of the Study include the Principal Investigator and the research staff supporting the Study; your City of Hope physicians and the health care team; the Health Information Management Services Department (i.e., Medical Records Department), and

affiliated research doctors and other medical centers participating in the research, if applicable. This also includes any agents or contractors used by these individuals or groups for purposes of conducting or managing this Study. At the City of Hope, the Institutional Review Board ("IRB"), and other City of Hope research regulatory committees will have access to your PHI as necessary to monitor research.

You are also allowing your PHI to be shared with the Office for Human Research Protections ("OHRP") and with any person or agency as required by law. In addition, certain other regulatory agencies, including the Food and Drug Administration ("FDA") and the National Cancer Institute ("NCI") will have access to your PHI.

Use and disclosure of your PHI may also continue for as long as the sponsor needs to maintain the PHI for purposes of obtaining approval of the use of leflunomide from the FDA or for other FDA reporting.

This study also involves tissue banking (storing your specimens such as blood). The tissue banked as part of this study will be for COH tissue banks**.** The banked tissue will be stored indefinitely.

This authorization will allow us to use and share your PHI for the Study. No other additional uses and disclosures other than for the purposes of the Study is included in this authorization. City of Hope's Notice of Privacy Practices will continue to protect your non-Study information. If necessary, another separate permission will be obtained from you for any non-Study uses or sharing of your PHI.

IV. **Expiration of this Authorization**: This authorization to use and share your PHI will expire twenty-five (25) years from the date that you sign this authorization.

V. **Further Sharing of Your PHI**: Your privacy is important and this is the reason for having rules which control who can use or see your PHI. City of Hope maintains control over your PHI at present, but once we share this information with a third party (for example, an individual or agency outside of the City of Hope), then it is no longer possible to maintain the same level of protection. The persons outside

our control may not be governed by federal or state privacy laws and it is possible that they could share your PHI with others for whom you have not given permission.

The information from this Study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential.

VI. **<u>Your Rights Under this Authorization</u>**: You may cancel this permission to use and share your PHI at any time by contacting City of Hope's Privacy Officer at (626) 256-HOPE (4673) ext. 64025. You should ask for the form, *Revocation (Cancellation) of Authorization for Use of Protected Health Information for Research*. Fill this form out and return it as the form instructs. Your cancellation begins when the Health Information Management Department of City of Hope receives this form. If you cancel this authorization to use and share your PHI, you will no longer be able to participate in the Study. This is because the research under this Study cannot be conducted without your PHI.

Once you cancel your permission to use and share your PHI, the researchers and others involved in conducting the Study will no longer be able to use or share your PHI for this research. PHI already used and shared up to this point as part of this Study will continue to be used for purposes of this research. This means that any uses of your PHI and any PHI shared about you by City of Hope prior to receiving your cancellation (revocation) form cannot be taken back. While no further PHI about you will be shared for the Study, your PHI already shared will continue to be used in the overall Study.

VII. **<u>Signing this Authorization is Your Choice</u>:** Your ability to obtain care at the City of Hope will not be affected by your decision to sign this authorization form. You will be able to continue to receive health care at City of Hope if you choose not to sign this authorization form or if you sign this form and later cancel your permission to use and share your PHI.

If you agree to the use and sharing of your PHI, please sign below. You will be given a copy of this authorization form.

_____ _____ _____

Research Participant's Signature Date Time

(date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

NOTE: To determine who should sign below, review the guidance document, *Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?*

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

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Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name