SUMMARY OF CHANGES – Consent

NCI Protocol #: TRC-10446
Local Protocol #: TRC-10446
Protocol Version Date: June 4, 2020

Protocol Title: Tocilizumab in Hospitalized Cancer Patients with Coronavirus 2019 (SARS-CoV-2) and Severe Complications of Coronavirus Disease 19 (COVID-19)

Informed Consent Version Date: June 4, 2020

Summary of Changes

Protocol Changes by Principal Investigator:

#	Section	Comments
1.	Global	The version date was updated. No additional changes were made to the informed consent.

Research Study Informed Consent Document

Study Title for Participants: Tocilizumab for Patients with Cancer and COVID-19 Disease

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
TRC-10446: Tocilizumab in Hospitalized Cancer Patients with Coronavirus 2019 (SARS-CoV-2) and Severe Complications of Coronavirus Disease 19 (COVID-19) (NCT04370834)

Overview and Key Information

What am I being asked to do?

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have severe COVID-19 pneumonia and have an underlying cancer diagnosis.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question: can tocilizumab be administered to cancer patients with severe COVID-19 lung disease? The trial provides access to tocilizumab for cancer patients who are unable to participate on the company sponsored randomized phase 3 trial comparing tocilizumab to placebo in severe COVID-19 disease.

What is the usual approach to my COVID-19 diagnosis?

There is currently no standard approach for patients with COVID-19. Many different therapies and supportive care (like receiving oxygen) are being used to take care of patients with COVID-19, and there are other clinical trials testing new therapies. There are currently no approved treatments for COVID-19 pneumonia.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for COVID-19, while continuing to get care that helps relieve any discomfort.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get tocilizumab for up to 2 doses. After the first dose, your symptoms will be assessed, and the doctors will decide if an additional dose may help you. If you are currently undergoing any treatment for your cancer, that treatment can continue, as long as your doctors decide it is safe.

This study is only available for patients who are already hospitalized for COVID-19. You will have study procedures daily until discharged (based on your study doctor's decision), until you decide to stop participating in this study, or until your death. After you are discharged from the hospital, your doctor and study team will watch you for side effects for at least 60 days after you receive tocilizumab. If you are discharged from the hospital sooner than 60 days, your doctor and study team may follow up with you by telephone for the remaining time and for up to a year, as long as any side effects you experienced after receiving tocilizumab have cleared up completely.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the tocilizumab may not help in improving your COVID-19 pneumonia.

There is also a risk that you could have side effects from the tocilizumab. These side effects may be worse and may be different than you would get with the usual approach for COVID-19 pneumonia.

Some of the most common side effects that the study doctors know about are:

- Can cause abnormal liver function tests and allergic reaction

There may be some risks that the study doctors do not yet know about.

Benefits

Your health may or may not improve in this study, but the information that is learned may help other people who have a similar medical condition in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you leave this study, you will not lose access to any of your regular care. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (the National Cancer Institute [NCI]). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to evaluate the impact of the drug called tocilizumab on COVID-19. Tocilizumab could help improve symptoms of COVID-19 pneumonia, but it could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drug will improve COVID-19 pneumonia in patients with cancer.

Tocilizumab has not been approved by the U.S. FDA for the treatment of COVID-19 pneumonia. The use of this drug in this study is experimental.

There will be about 217 cancer patients taking part in this study.

What are the study groups?

In this study, there will be two study groups.

- Cohort A – Not on mechanical ventilation and no imminent risk of requiring it
- Cohort B – On or at risk for needing mechanical ventilation

Treatment schedule: Both groups will receive the same treatment. You will get tocilizumab through your vein or central line over 1 hour. You will be closely watched by the study doctors. Between eight hours and 7 days after completion of the first dose, a second dose may be given to you if the doctors do not see an improvement in your symptoms, specifically, your fever. A second dose may also not be necessary if you have improvement after the first dose.

Treatment is intended for a maximum of 2 doses only.

What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Vital signs including the level of oxygen in your blood prior to receiving the study drug, then at least every 24 hours while you are in the hospital and once you are off the study.
- Blood counts prior to receiving the study drug, and every 24 hours while you are in the hospital . Optional blood counts may also be done every 12 hours for four times after your first dose of tocilizumab and once you are off the study.
- Liver function tests prior to receiving the study drug, and then optional liver function tests every 12 hours for four times after your first dose of tocilizumab and once you are off the study.
- Chest X-rays prior to receiving the study drug, and when your condition requires them as judged by your study doctor.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

You may have optional blood samples taken for the study. These samples will be used to evaluate changes in your cytokine levels associated with getting tocilizumab and to assess the amount of tocilizumab in your blood. We will also look at how much of the SARS-CoV-2 virus is in your blood. These samples will be taken prior to you receiving the study drug, every 12 hours four times after the first dose, at 72 hours after your first dose of tocilizumab, and 7 days after your first dose of tocilizumab if you are still in the hospital. See the section "Optional studies that you can choose to take part in" for more information on these blood collections.

For children under 12 years of age, less blood will be drawn. All of these blood draws are optional.

A patient study calendar is attached at the end of this document. It shows how often these procedures will be done.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that the tocilizumab may not be as good as the other approach or study drug at stabilizing your COVID-19 pneumonia.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The study drug used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for at least 28 days after you have completed the study.

Blood Draw Risks

Some of the risks from drawing blood from your arm may include pain, bruising, light-headedness, and rarely, infection. For most people, needle punctures to get blood samples do not cause any serious harm. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Side Effect Risks

Tocilizumab used in this study may affect how different parts of your body work such, as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drug.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of Tocilizumab (Table Version Date: April 14, 2020)

The side effects associated with tocilizumab that have been reported in clinical studies for various medical conditions are listed below. There may be side effects that are not known at this time. The risks associated with short-term use of tocilizumab in subjects with COVID-19 are unknown.

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving tocilizumab (RO4877533), from 4 to 20 may have:
• Infection

RARE, AND SERIOUS In 100 people receiving tocilizumab (RO4877533), 3 or fewer may have:
• A tear or hole in internal organs that may require surgery which may cause pain, difficulty swallowing • Liver damage which may cause yellowing of the eyes and skin • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Additional Drug Risks

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant within 28 days after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your COVID-19 pneumonia. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the tocilizumab ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The optional research blood tests.

You or your insurance provider will not have to pay for the tocilizumab while you take part in this study.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor (NCI) and the company (Genentech/Roche) supporting the study or the study agent now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works to conduct research.
- The NCI and the groups it works with to review research.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with COVID-19 pneumonia in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about COVID-19 pneumonia using blood samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Known future studies

If you choose to take part in this optional study, researchers will collect additional blood for research on the effect of tocilizumab on the "cytokine storm" caused by your COVID-19 pneumonia. Your blood will be measured for levels of IL-6, the immune system protein that tocilizumab blocks, and other proteins that make up the cytokine storm. Researchers will measure changes in the levels of these proteins and evaluate your COVID-19 pneumonia and how much of the SARS-CoV-2 and tocilizumab is in your blood.

Unknown future studies

If you choose to take part in this optional study, blood left over from the known future studies described above will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Nationwide Children's Hospital in Columbus, Ohio, and is supported by the NCI. Also, any health-related information, such as your response to treatment, results of study tests, and medicines you took, will be stored for future use. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code.

Changes in your genetic code may be passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

What is involved in this optional sample collection?

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

1. About 3 teaspoons of blood will be collected from a vein in your arm before your first dose of tocilizumab, every 12 hours four times after your first dose of tocilizumab, 72 hours after your first dose of tocilizumab, and 7 days after your first dose of tocilizumab if you are still in the hospital. Pediatric patients will only have blood taken twice during the "every 12 hours four times after your first dose of tocilizumab" collections.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance.

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. Only your study doctor and a few study researchers will have access to the master list linking the code numbers to names. The biobank and the genomic sequencing laboratory will receive your samples with the following information only: your sample code number;

your age, race/ethnicity, and gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance for exams, tests, and procedures done for research purposes only; these include the blood draws and biobanking of your specimens. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I need my blood samples to be returned?

Blood samples that remain in the biobank can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be returned if needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Blood samples and genetic material (DNA and RNA) that are no longer in the biobank or that have already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory studies described above.

YES NO

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Patient Study Calendar

	Baseline	Day 1	Every 12 Hours four times following first dose of tocilizumab	Every 24 Hours until hospital discharge	72 hours after initial treatment	7 days after initial treatment[c]	Off Treatment[a]
Tocilizumab[A]		X					
Pre-study procedures including Informed consent, Demographics, Medical history, Pregnancy test*, Height, Weight, BSA and BMI	X						
Concurrent meds	X	X----------X					
Physical exam and Performance status	X						
Vital signs	X			X			
COVID-19 testing	X						
Test to measure amount of oxygen carried by red blood cells	X			X			
Blood draws for complete blood count and general health status	X		X[b]	X			X[b]
Blood tests to evaluate organ function	X						
Blood clot tests	X		X[b,d]				X[b]
Side effect evaluation	X	X----------X					
Chest X-Ray (as clinically indicated)[d]	X						
Blood collection for research purposes to test your immune response and amount of SARS-CoV2 and Tocilizumab in your blood[b]	X[b]		X[b]		X[b]	X[b]	

A: Tocilizumab: Dose as assigned.
a: Off-treatment evaluation.
b: Optional. A total of 3 tablespoons of blood will be taken for the research and general health blood collections. Your doctor may collect blood for general health status more frequently than listed here.
c: Only if you are still in the hospital.
d: Only 2 collections will be done if you are less than 18 years old.
*For women of childbearing years only if you or your doctor think it is needed.