Official Title	Ganciclovir to Prevent Reactivation of Cytomegalovirus in Patients with Acute Respiratory Failure and Sepsis
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NAME OF INSTITUTION/MEDICAL CENTER

Consent to Participate in a Research Study Called:

Ganciclovir to Prevent Reactivation of Cytomegalovirus in Patients with Acute Respiratory Failure and Sepsis

Who is in charge of this research study?

Principal Investigator:

Name Title Area Code XXX Phone number

Co-Investigators:

Research Staff:

Emergency number (24 hours): [000-000-0000]

Note: If you are serving as a legally authorized representative, the terms "participant", "you", and "your" refer to the person for whom you are providing consent.

Doctors at [insert site] are conducting this study. This study is funded by the National Institutes of Health (NIH) National Heart, Lung, & Blood Institute (NHLBI).

Important things to know about this study

You are invited to participate in a research study. The purpose of this research is to find out if a drug called ganciclovir can prevent cytomegalovirus (CMV) reactivation, in which the virus wakes up from an inactive state, in patients with respiratory failure associated with severe sepsis.

People who agree to join the study will be asked to take part in study procedures for 28 days, or less if discharged from the hospital before that time. The study involves infusion of either ganciclovir or placebo and collection of blood and throat/lung fluid samples. A follow-up phone call and a survey will be requested 6 months later. You may withdraw from this study at any time. If you choose to withdraw, we will continue to access clinical information related to study outcomes unless you specifically opt out.

We do not know if Ganciclovir would help prevent CMV reactivation, and it could even make your condition worse. Ganciclovir could cause side effects such as low levels of white blood cells, as described below in this form.

You do not have to join this study. You can choose to receive standard clinical care instead of participating in this study. We will give you details about the purposes, procedures, risks and

possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

What is the purpose of this consent form?

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to enroll in the study or not. This process is called 'informed consent.' We will give you a copy of this form for your records.

Why is this research study being done?

You are being asked to participate in this research study because your physicians have determined that you have respiratory failure requiring high-level respiratory support and you also have an overwhelming response to severe infection (severe sepsis). Respiratory failure (severe lung failure) is a life-threatening disease. Lung failure means the lungs have trouble carrying out their normal function of getting oxygen into the blood and removing carbon dioxide from the body.

In order for you to take part in this study, we verified that you also have previously had an infection with a virus called Cytomegalovirus (CMV). CMV infection is very common and over half of the adults in the US have been infected. Once you have had a CMV infection, CMV remains in your body and can later become active again. In people who are critically ill, CMV tends to be reactivated in the lungs and blood. This CMV reactivation may cause further lung problems in patients associated with severe sepsis resulting in longer hospital or intensive care unit (ICU) stays and needing more time on a breathing machine.

Ganciclovir is an FDA approved drug that has been widely used for the prevention and treatment of CMV in patients with weakened immune systems. We want to study the use of ganciclovir for the possible prevention of CMV reactivation in patients with respiratory failure associated with severe sepsis.

A total of 500 patients will be enrolled in this study at sites throughout the US.

You will be assigned to a study group

If you decide to take part in this study you will be assigned to receive either ganciclovir or placebo (a solution that does not contain any active medications). Both will be given intravenously (by IV). You will receive "study drug" (ganciclovir or placebo) twice daily through Study Day 5, once daily through Study Day 28 or until you have been discharged,

whichever comes first. If you are randomized to ganciclovir, you will receive the standard dose based on your body weight and kidney function.

There is an equal chance of receiving either ganciclovir or placebo. Which of these you will receive is decided at random (by chance, like the flip of a coin). This process is called randomization. Neither you nor the study team will know which treatment you are receiving, but there is a procedure in place for your study doctor to find out this information if needed. No matter which group you are assigned to, you will still receive the standard treatment that your medical center provides for patients with your condition.

If you are discharged from the hospital before Study Day 28, the study drug or placebo will be discontinued.

Pregnant women may not take part in this study. Routine pregnancy tests are often done when women are admitted to the ICU. If you are a woman who is able to become pregnant and a pregnancy test was not done, we will test for pregnancy before you receive any study drug. Another pregnancy test will be done on study day 7 or when you are discharged from the hospital, whichever is earlier.

What will happen during the study?

Blood Draws:

We will monitor your lab results during the course of the hospital stay. Whenever possible, we will use results from blood tests that were already drawn as part of your routine care, rather than drawing extra blood. In the event we need to draw additional blood, there will be no charge to you. Each sample will be approximately between 4 and 44 ml (½ and 9 teaspoons) of blood, depending on the day. Blood samples will be obtained upon enrollment into the study and twice weekly until your last dose of study drug.

Usually, the blood will be drawn from an IV line already placed as required for care. If no such IV is present, blood will be drawn through a small needle.

We will use this blood for safety testing, pregnancy, to check for CMV and other viruses, and to look at markers that are related to your infection and your body's response to the infection. The total amount of blood collected during this study will be no more than 200 ml (about ¾ cup).

Endotracheal (ETT) Aspirations:

Endotracheal (ETT) Aspiration is a procedure that is commonly performed to help clear excess respiratory secretions. If this procedure is performed, a sample will be collected through the endotracheal tube, or breathing tube, and sent to the laboratory for testing of CMV and other viruses. ETT aspiration samples may be collected at day 1 of study and every fourth day while you are still on the breathing machine.

Survey:

You will be asked to complete a survey after 6 months have passed. It may take about 15 minutes to complete. You do not have to answer any questions you do not want to answer. If you decide to not complete the survey, you can still participate in this study.

Leftover Specimens:

If there are leftover samples, including samples of lung fluid after a bronchoscopy, biopsy samples, or any leftover specimens related to your illness that were collected before you enrolled in this study or for clinical reasons during the study, we will also use these to test for CMV.

In the event that an autopsy is performed, a small sample of your lung tissue may be requested.

Follow Up Phone Calls

You may receive one or two follow up phone calls for this study. If you are discharged early in the study, you will receive a phone call on Day 28. All participants will receive a phone call after six months. During these phone calls we will ask about your health, document any serious health problems, and collect details about any hospital admissions. We may also obtain hospital records or other health records. Your involvement in this study will end after the six month phone call.

Optional Follow Up

With your permission, the study staff may also contact you to ask if you would be willing to participate in additional study activities after hospital discharge. At the end of this consent form, we will ask you to indicate whether or not you would agree to be contacted for additional study activities.

The following table shows what will happen at each study day.

Table of activities

Study Day	Screening	Day 1	Day 4	Day 7	Day 11	Day 14	Day 18	Day 21	Day 25	Day 28	Day 180
Consent	X										
Pregnancy Test	X			A follow-up pregnancy test will be done at day 7 or at time of hospital discharge, whichever is earlier							
Blood draw	X	X	X	X	X	X	X	X	X	X	
ETT aspiration		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	
Receive study drug/ placebo		Twice daily through Day 5		Once daily, day 6 through day 28, or until hospital discharge whichever is earlier							
Check on health status		X	X	X	X	X	X	X	X	X	X*
Survey											X

(X) Only some participants will receive this procedure on these days of the study. Ask your study doctor if you have questions about the additional monitoring and if it would apply to you.
*Follow up phone call

What are the side effects (risks)?

Ganciclovir

It is estimated that tens of thousands of persons have received IV ganciclovir (or its oral form, valganciclovir) over the last ~20 years.

- The primary side effect seen with use of ganciclovir is low levels of white blood cells. When the levels of white blood cells are low, there is an increased risk of infection. Low levels of white blood cells have generally been seen after months of drug exposure and in patients receiving other drugs that affect white blood cell production. Low levels of white blood cells are not often seen in critically-ill patients.

- The following events have been reported infrequently in trials that compare ganciclovir with no treatment or other drugs. For most of these events, there was no difference in occurrence between the people who received the drug and those who had no treatment or another drug. These events include:
    - low levels of red blood cells and/or platelets

  - fever
  - loss of appetite
  - raised liver enzymes
  - headache
  - confusion or hallucination
  - seizures
  - insomnia
  - nerve damage of hands/feet
  - pain and inflammation at injection site
  - sweating
  - rash and itching
  - problems with kidney function;
  - infertility
  - diarrhea

- Ganciclovir has been shown to cause cancer in laboratory animals. Although there is no information that ganciclovir causes cancer in humans, a risk cannot be ruled out.

- As with any medication, it is possible that you could have an allergic reaction to ganciclovir. The reaction may include, but is not limited to, a rash, swelling, or difficulty breathing. You will be watched closely for these symptoms when you receive the study drug, and appropriate medical care will be given if your study doctor thinks you might be having an allergic reaction.

- Taking Ganciclovir may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. You should not become pregnant or father a baby while on this study. Women should not breastfeed a baby while on this study. If you are male, it is important to understand that you need to remain abstinent or use effective birth control while receiving study drug and for up to 3 months after receiving the last dose of study drug. If you are female, it is important to understand that you need to remain abstinent or use effective birth control while receiving study drug and for up to 1 month after receiving the last dose of study drug. If you become pregnant within 1 month after the last study drug dose, you must inform your study doctor immediately.

- As with any medication, there may be additional side effects, including death, which we don't know about. It is not possible to predict in advance if any of the above problems or other problems will develop, but if they do the study medication will be stopped and appropriate care will be provided to you.

- One of the tests conducted at the start of this study is an investigational test for CMV infection. There is a small risk that the test could register a 'false positive,' which means the results say you are CMV positive when you are not. An approved CMV test will also be used with results returned within 2-3 days. If during those 2-3 days you receive Ganciclovir, your risk of experiencing side effects is minimal. If it is found that there was a false positive, Ganciclovir dosing will be promptly stopped and we will monitor your health for 2 days after the last dose.

The following table shows information about the most serious possible side effects of ganciclovir and what the risks are expected to be for patients who take part in this study. Note that none of the side effects below were seen in a similar study with ganciclovir that took place prior to this one.

Summary of side effects			
Side effect	Seen in humans?	Reported in other trials?	Expected increased risk in this trial?
Low levels of white blood cells	Yes	Yes	Yes <2%
Low levels of platelets	Yes	No	No
Low levels of red blood cells	Yes	Yes, only in patients with HIV	No
Problems with kidney function	Yes	Not seen in recent trials	No
GI problems	Yes	Yes	No
Cancerous tumors	No	No	No
Birth defects	No	No	No

Risks of Endotracheal Aspirates

ETT aspiration is routinely performed on intubated patients by respiratory therapy as part of their clinical care routine to help clear respiratory secretions. There are no known risks to this procedure and it would be considered inappropriate care if this procedure was **not** performed.

Other

Whenever possible, any lab work needed will be obtained from results already drawn for your clinical care. If blood needs to be drawn, we will draw it from an IV already in place. If the blood must be obtained by a needle stick, there is the risk of pain, bruising, redness or swelling and, in rare cases, infection at the site where the needle is inserted.

What are the benefits?

There may be no direct benefit to you for participating. If ganciclovir reduces the amount of time patients with severe sepsis remain on respiratory support this may benefit you. Also, future patients may benefit if ganciclovir proves beneficial in the prevention of CMV disease reactivation in patients with sepsis-related lung failure.

Will you pay me to be in this research study?

Being in this study is voluntary. There is no payment for being in this study. The research done with your tissue and/or blood may help to develop new commercial products in the future. There are no plans to pay you should this occur.

Will it cost me to be in this research study?

You will not be financially responsible for the cost of treatment or procedures if they are done only for this study. This includes the costs of study medications, extra laboratory tests, physician assessments, or outpatient clinic visits. You or your insurance company will be responsible for the costs of regular treatment not performed for the purpose of this study. If you have questions about your bills and health insurance coverage, call the financial service department at the medical center where you will be treated.

What will happen if I get sick or hurt while in this study?

For a life threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact [FILL IN AS APPROPRIATE]. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

What are my options if I am not in the study?

You do not have to join this study. You are free to say "yes" or "no". Your regular medical care would not change if you decide to say "no".

You have other choices for treatment. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices

There are no currently approved drugs to prevent or treat CMV reactivation specifically in patients with respiratory failure associated with severe sepsis. The alternative to being in the study is to just receive standard clinical care.

Termination of the Study

If you are unable to consent for yourself when you are first enrolled in this study, your legally authorized representative will be your surrogate. When you are able to provide consent, you may refuse further participation in the study. You may also change your mind about being in the study at any other time. We may be required to monitor your health for a period of time after you withdraw from the study. Your study doctor will discuss this with you. Whether or not you choose to be in this study, it will not affect your care here at [medical center].

Your study doctor may decide to take you off this study if the study drug appears to be harmful to you, if you fail to follow the instructions for study, if you become pregnant during the study, if it is discovered that you did not meet the study requirements, or if the study is cancelled.

During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn this kind of information, we will tell you. If you want to find out whether you received study drug or placebo, you can contact the study doctor at [phone number] after the entire study has been completed. During this study, we do not expect any test results that would affect your care, so we do not plan to return results to you.

Protecting your privacy

In order to get the results of the research study, the researchers and study staff at the Fred Hutchinson Cancer Center, the University of Washington, and the U.S. National Institutes of Health (NIH) National Heart, Lung, & Blood Institute (NHLBI) (the study funder) will need to review your research records. Only authorized people will see your research records. People who look at your records will be very careful to protect your name and identity. Research records are kept in locked files and kept indefinitely. We may write reports and give talks about this study. If we do, we will not use your name or share anything that would let others know who you are.

Certain people look at the records to be sure that we are doing the study in the right way. They also make sure that we protect your rights and safety. These may include the following institutions and their representatives or agents:

- [site name]
- Fred Hutchinson Cancer Center (Fred Hutch)
- Institutional Review Boards (IRB) of the above institutions
- National Institutes of Health (NIH), U.S. Office for Human Research Protections (OHRP), and U.S. Food and Drug Administration (FDA)
- Researchers involved in the study, including independent monitors

Some tests for this study are done at laboratories outside of [medical center]. Samples sent to these labs will not include your name. They will be labeled with study numbers instead.

[If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.]

After we do tests on your study specimens and after your clinically ordered tests have been completed, there may be leftover material. We would like you to donate these leftover specimens for future research. The information that identifies you will first be removed from your information or tissue samples. Other data and samples collected for the study will be stored for future research, but only after identifiable information is removed. Genetic testing into the causes of acute respiratory failure, factors linked with acute respiratory failure outcomes, and factors linked with ganciclovir treatment may be performed on your de-identified data. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Your donated specimens will be stored at the laboratories at Fred Hutch in Seattle, Washington. They will be used for research only. Researchers will not report their results to you or your study doctor. The research results will not appear in your health record. They will not affect your care.

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums. GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

This research is covered by a Certificate of Confidentiality from the U.S. government. This Certificate helps protect the confidentiality of information about people who join this study. If you join the study, the Certificate means that generally we would not have to give out identifying information about you even if we were asked to by a court of law. We would use the Certificate to resist any demands for identifying information.

We could not use the Certificate to withhold research information if you give written consent to give it to an insurer, employer, or other person.

This protection has some limits. We would voluntarily provide the information:

- To a member of the federal government who needs it in order to audit or evaluate the research.
- To the funding agency and groups involved in the research, if they need the information to make sure the research is being done correctly.
- To the federal Food and Drug Administration (FDA), if required by the FDA.
- To someone who is accused of a crime, if he or she believes that our research records could be used for defense.
- To authorities, if we learn of child abuse, elder abuse, or if participants might harm themselves or others.

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.

Whom should I call if I have questions or research study problems?

If you have questions about:	**Call:**
This study (including complaints and requests for information)	[000-000-0000] (Dr. [full name of PI]) [000-000-0000] ([name and title of research staff contact])
If you get sick or hurt in this study	[000-000-0000] (Dr. [surname of PI])
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) [include local IRB contact information if applicable]
Your bills and health insurance coverage	[000-000-0000]

CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

I have carefully read this consent form. This study has been explained to me. I have a choice about whether or not I will take part in this study. I have been told of the risks and benefits of taking part in this study. I have had the chance to ask questions about it, and all questions were answered to my satisfaction. I am to receive a signed copy of this form. I now agree to take part in this research study.

I also give permission to the people and organizations connected with this research study to review and copy my research records.

Earlier in this consent form, we told you that the researchers may wish to contact you for additional study procedures after hospital discharge.

Please **INITIAL** in the box below next to the **ONE** option you choose.

_____ **I agree** to be contacted to consider additional study procedures after hospital discharge.

or

_____ **I do not agree** to be contacted about additional study procedures after my hospital discharge.

_____ _____
Research Participant Date

_____
Type or print name of Participant

Legally authorized representative:
Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask questions;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to consent on behalf of the participant for him or her to participate in this study.

Legal Representative Signature	Date
Type or Print Name of Legal Representative	Type or Print Name of Participant
Relationship to Participant	

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

_____	_____	_____
Printed Name	**Signature**	**Date**

Please read the question and circle YES **or** NO**.**

Do you agree to allow the study team to continue to monitor your clinical data (i.e. look at your medical record to collect important outcomes about your ICU stay) even if you choose to withdraw from the study and stop receiving study interventions or procedures? (circle one)

YES NO Initials: _____ Date:

CONTINUING CONSENT

Due to the nature of my illness, my legally authorized representative gave consent allowing me to take part in this research. I am now able to understand the purposes, procedures and risks of this research study. I have had a chance to ask questions and volunteer to continue with participation in this study.

_____ _____

Research Participant Date

_____

Type or Print Name of Participant

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

Printed Name	**Signature**	**Date**

Please read the question and circle YES **or** NO**.**

Now that you are able to consent, do you agree to allow the study team to continue to monitor your clinical data (i.e. look at your medical record to collect important outcomes about your ICU stay) even if you choose to withdraw from the study and stop receiving study interventions or procedures? (circle one)

YES **NO** Initials:_____ Date:

MEDICAL STAFF PERSON'S STATEMENT

I have discussed the above research study, including the study purpose, procedures, risks and benefits, and possible alternatives, with the person signing above. All the elements of informed consent were reviewed and discussed with the subject. Special concerns that the participant expressed were noted and appropriately addressed. I encouraged questions and have answered all questions to the best of my ability. The participant is aware that he/she has a choice in taking part in this study. A signed copy of the consent form will be given to the participant.

_____	_____	_____
Printed Name and Title of Medical Staff Person	Signature of Staff Person	Date

_____

Signature of Additional Staff Person Present During Consent Process (if present)