The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title: Letermovir for Cytomegalovirus Prophylaxis in Patients with Hematological Malignancies Treated with Alemtuzumab

Principal Investigator: John Reneau, MD, PhD

Sponsor: The Ohio State University

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study
The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

You are invited to take part in a clinical trial, a type of research study, because you have one of several types of blood cancers, you have not undergone an allogenic hematopoietic stem cell transplant (HSCT) in the last 6 months, your doctor intends to treat you with alemtuzumab, and you have been previously exposed to cytomegalovirus (CMV). Patients receiving this treatment can experience a reactivation of the CMV infection (when patients who had no symptoms of infection begin experiencing symptoms of active infection again), and this possibility prevents wider use of alemtuzumab, which is an otherwise well-tolerated

treatment. Successfully preventing a reactivation of CMV could allow doctors to offer more patients alemtuzumab.

A drug called letermovir has been approved for preventing CMV reactivation in patients who have received HSCT. In this study, letermovir will be tested to determine if it is safe and effective in patients being treated with alemtuzumab and who have not received HSCT in the last 6 months.

You will continue to take letermovir during your treatment with alemtuzumab, and for 3 months after completing alemtuzumab. We will follow up with you once, about 30 days after your last dose of letermovir. You will undergo several medical procedures during this study, including: blood draws, physical exams, pregnancy tests, and taking the study medication.

The most common side effects while taking letermovir are nausea, diarrhea, vomiting, swelling in your arms and legs, cough, headache, tiredness, and stomach (abdominal) pain. It is extremely important that you, any caregivers, and other healthcare providers have the correct study team contact information for safety and management of toxicities. To address this, Trial Alert Cards have been created to record study team phone numbers, with a 24-hour option, and come in a size that can be carried in your wallet. The cards include a note to healthcare providers asking them to contact your treating physician, in case you seek care with anyone unfamiliar with the trial. You will receive this card at your first/ next visit, please keep it with you at all times.

You may or may not benefit from participating, but the information gained in this study may help doctors treat patients in the future.

You do not have to take part in this clinical trial, and may still receive cancer care at The Ohio State University without taking part.

1. Why is this study being done?

You are invited to take part in a clinical trial, a type of research study, because you have one of several types of blood cancers, and your doctor intends to treat you with alemtuzumab. The study doctors at Ohio State are testing a drug, letermovir, which will be given to you once a day during your normal treatment, and for 3 months after completing alemtuzumab.

Merck is supporting this research study by providing the study drug, letermovir.

The purpose of this research is to determine how safe and effective (how well something works) letermovir is in preventing reactivation of cytomegalovirus (CMV). This study will also be testing how effective letermovir is when taken with alemtuzumab.

Letermovir is approved by the United States Food and Drug Administration (FDA) for the prevention of CMV reactivation in patients who have received an allogenic hematopoietic stem cell transplant (HSCT), but it has not been approved for non-transplant patients.

This study is being done to determine if letermovir is effective in preventing CMV reactivation in non-HSCT patients treated with alemtuzumab.

2. How many people will take part in this study?

At the Ohio State University, approximately 30 people will take part in this study.

3. What will happen if I take part in this study?

If you decide to take part in this research study, you will first be asked to sign this consent form.

Screening

After signing the consent form, you will have tests and procedures completed to determine if you can participate in the study. Some of these may be completed as part of your standard medical care. They include:

- Medical history: A review of your complete medical history, lab results, including any medications/supplements you have used or are using now.
- Pregnancy test (for females of childbearing potential only): A blood or urine sample will be taken, as part of your routine care, to see if you are pregnant. Additional details about contraception while participating in this study can be found in Section 6 (Pregnancy) of this informed consent form.
- Physical exam: The doctor will do an overall review of your current health, which includes recording your vitals (blood pressure, heart rate, respiratory rate, temperature), height, weight, and ECOG performance status (a measure of how well you are feeling). Your doctor will also look for and ask you about common signs of CMV infection.
- Blood will be collected for standard of care medical testing, as well as for HIV, Hepatitis, and CMV testing. Blood tests will include the following:
    - CBC (complete blood cell count) with differential: A test to measure the number of red blood cells, white blood cells, and platelets in the blood, including the different types of white blood cells (neutrophils, lymphocytes, monocytes, basophils, eosinophils).
    - CMP (comprehensive metabolic panel): A group of 14 tests that measures several different substances in your blood to give information about the current status of your body's metabolism, including your blood sugar (glucose) levels, the balance of electrolytes and fluid in your body, and the health of your kidneys and liver.

  - Prothrombin time (PT-INR): A test to measure how long it takes for a clot to form in a blood sample. An INR (international normalized ratio) is a type of calculation based on PT test results.
- You will be assessed for any adverse symptoms you are experiencing at baseline before your first dose of letermovir.

Treatment Procedures: (occur after you have been enrolled into the study)

If you are eligible for this study and choose to participate, you will undergo the following procedures while you are undergoing alemtuzumab treatment.

- Physical exam: The doctor will do an overall review of your current health, which includes recording your vitals, height, and weight. Your doctor will also look for and ask you about common signs of CMV infection.
- Your doctor will review your lab results, and confirm any medications or supplements you have used or are using now.
- Pregnancy test: A blood or urine sample will be taken, as part of your routine care, to see if you are pregnant (if you are a woman who is able to become pregnant).
- Blood will be collected for standard of care medical testing and CMV testing.

If you experience CMV reactivation while you are on study, all of these procedures will be repeated. At that time, you will also have additional blood drawn to look for any mutations in the CMV genes.

- You will be assessed for any adverse events.

Study Drug

- Within days of your treatment beginning, you will also receive your letermovir. It is an oval tablet that you will take once a day. You should swallow it whole, and you can take it with or without food.
- You should take letermovir at the same time every day. If you miss a dose, take it as soon as you remember. If it is more than 18 hours late, skip that dose, and take your next dose at your regularly scheduled time. Do not double your dose to "make up" for the missed one.
- While taking letermovir (from 2 weeks before treatment until 72 hours after your last dose), you must avoid eating grapefruit and Seville oranges or drinking their juices and other quinine-containing drinks or foods.
- If for any reason, you are unable to take letermovir by mouth for an extended period of time, you will be able to receive it through your vein (intravenously).

Follow-up

About 30 days after your last dose of letermovir, you will be seen again by the study team, and you will have the following procedures:

- Physical exam: The doctor will do an overall review of your current health, which includes recording your vitals, height, and weight. Your doctor will also look for and ask you about common signs of CMV infection.
- Your doctor will review your lab results, and confirm any medications or supplements you have used or are using now.
- Pregnancy test: A blood or urine sample will be taken, as part of your routine care, to see if you are pregnant (if you are a woman who is able to become pregnant).
- Blood will be collected for standard of care medical testing and CMV testing.

If you are having ongoing side effects, or you had CMV reactivation, your study doctor will continue to follow you and provide appropriate medical care until resolved.

4. How long will I be in the study?

Your participation in this study begins once you sign this consent form, and will continue through 30 (+/- 7) days from the last dose of letermovir. The study team may continue to follow up with you after that time if you are having any side effects related to study treatment.

You may have to discontinue treatment early if:

- You experience intolerable or unacceptable side effects
- You do not follow dosing instructions or other requirements of the trial
- Your doctor feels that continuing on the study would place you in greater than necessary risk.

You must discontinue study treatment if:

- You experience a CMV reactivation
- Your doctor feels it is in your best interests to discontinue
- (Female patients) You become pregnant

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with your study doctor if you have any questions.

Side Effects

The most common side effects while taking letermovir are:

- Nausea (27%)
- Diarrhea (26%)
- Vomiting (19%)
- Swelling in your arms and legs (14%)
- Cough (14%)
- Headache (14%)
- Tiredness (13%)
- Stomach (abdominal) pain (12%)

Other possible side effects while taking letermovir are:

- Tachycardia (fast heart rate) (3%)
- Atrial fibrillation (irregular heart rate) (3%)
- Anemia (low hemoglobin) that is life-threatening or needs urgent treatment (2%)
- Allergic reaction (<1%)

Talk to your study doctor for medical advice about side effects.

Pregnancy

We do not know the risks associated with pregnancy while taking letermovir. For this reason, you should not become pregnant, breast-feed, or father a child while you are on this study. Women who can get pregnant and men with partners who can become pregnant will be asked to practice a highly effective method of birth control while participating in this study and for 90 days after the last study therapy.

Highly effective birth control includes:

- True abstinence
- Intrauterine device (IUD)
- Diaphragm with spermicide,
- Contraceptive sponge,
- Condom,
- Vasectomy

OR

- Use of appropriate double barrier contraception.

Also acceptable methods:

- Hormonal (birth control pills, injections, implants)

Personal Information
Study doctors and the study team will take steps to ensure that information obtained about you for this study will be kept confidential to the extent required by U.S. or local law. However, there is still the potential risk of breach of confidentiality, patient identity, and privacy during the study.

Other risks
Obtaining blood samples may cause some discomfort, pain, bruising, and/or bleeding. You may feel lightheaded or faint, develop an infection with redness and irritation of the vein at the site where blood is drawn.

Your study doctor will closely monitor your health through this study and will discuss with you any questions regarding risks, discomforts, and side effects. If significant new findings are discovered during the study that could affect your willingness to continue to participate, this information will be reported to you as soon as possible.

If you have any concerns about this study at any time you should contact your study doctor.

7. What benefits can I expect from being in the study?

It is not possible to predict or guarantee that this treatment will benefit you. Even with letermovir treatment, you may still have a reactivation of CMV. This treatment may also be harmful to you. This study is an important step in developing a treatment and planning other studies that may help patients in the future.

8. What other choices do I have if I do not take part in the study?

You do not have to take part in this research study. You may receive the standard medical care for prevention of CMV reactivation while receiving alemtuzumab, participate in another clinical trial for prevention of CMV reactivation, or go without treatment for prevention of CMV reactivation.

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. What are the costs of taking part in this study?

The study drug Letermovir will be provided by Merck and not billed to you/your insurance company. In addition, you will not be charged for tests/procedures performed solely for research purposes.

The drug Alemtuzumab will be billed to you/your insurance, in the usual manner. Most of the care you receive on this study is considered routine for your condition, because you would receive it even if you were not participating in a clinical trial.

Participating in this research study may lead to additional costs to you. In some cases, it is possible that your insurance company will not pay for these costs because you are taking part in a research study. You and/or your insurance company will be billed for all tests or procedures that are considered to routine service for your condition. You will be responsible for any deductibles, coinsurance or co-payments required by your health plan. Before participating in this trial, we recommend that you ask your health plan if there are any limitations or restrictions to your coverage. Your study doctor or coordinator can tell you which costs are covered by the study.

10. Will I be paid for taking part in this study?

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

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects' research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information be used or shared for future research?

Yes, they may be used or shared with other researchers without your additional informed consent.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If we find information that significantly impacts your health, we will share it with you. If you have a CMV reactivation, your blood will be collected for CMV genotyping. Results of that will not significantly impact your health, but it may impact how your doctor wants to treat you, and they will discuss those findings with you if so.

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

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;

- Information gathered for this research about:
  - HIV / AIDS
  - Hepatitis infection
  - Other reportable infectious diseases
  - Physical exams
  - Laboratory, x-ray, and other test results
  - Diaries and questionnaires
- Records about any study drug you received;

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Merck, who is providing letermovir for this study.

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact **Dr. John Reneau at 614-293-3196 (office hours) or 614-293-8000 (24 hours)**.

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact:

HIPAA Privacy Manager
The Ohio State University Medical Center
600 Ackerman Road
Suite E2140

Columbus, OH 43202
614-293-4477

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact **the Office of Responsible Research Practices at 1-800-678-6251**.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact **Dr. John Reneau at 614-293-3196 (office hours) or 614-293-8000 (24 hours)**.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant**
	AM/PM
	Date and time
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
Relationship to the participant	**AM/PM**
	Date and time

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time