**Site Name**

**CONSENT FORM TO BE PART OF A RESEARCH STUDY**

**GROUP 2**

| | |
|---|---|
| **Title of Research:** | A Phase 1 Pharmacokinetic and Safety Assessment of Oral Letermovir in Infants with Symptomatic Congenital Cytomegalovirus Disease |
| **UAB IRB Protocol #:** | IRB-300009772 |
| **Principal Investigator:** | Site PI Name |
| **Sponsor:** | National Institute of Allergy and Infectious Diseases |
| **Sponsor Protocol #:** | DMID 21-0027 |

*For Children (persons under 18 years of age) participating in this study, the term "You" and "Your" addresses both the participant ("you") and the parent or legally authorized representative ("you").*

| | |
|---|---|
| **General Information** | You are being asked to allow your baby to take part in a research study. This research study is voluntary, meaning your baby does not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form. |
| **Purpose** | The purpose of this study is to determine the dose of a new medication (Letermovir) needed to treat babies diagnosed with congenital cytomegalovirus (cCMV). |
| **Duration & Visits** | Your baby will be in the study for 42 days.<br><br>Your baby will start taking the study medication on Study Day 1. The visits for Study Days 1, 5, 14, 21 and 42 will each take 1-2 hours. Visits on Study Days 2, 3, 4, 6, 7, 8, 9, 11, 12 and 13 will require you to bring your baby to the clinic to administer the study medication or someone from the study team will watch you mix and administer the medication in person or on video. These visits will each last about 30 minutes. The visit for Study Day 10 will include blood collection from your baby at 6 time-points over a 25 hour period. All study medication will be administered with your baby's formula. |
| **Overview of Procedures** | We will collect some baseline information about your baby (date of birth, gender, race, ethnicity, birth weight, current weight, length, and medical history). Your baby will take the medication by mouth once a day for 14 days. At each study visit, we will ask you questions regarding any issues that you have had giving your baby the medicine. While your baby is taking the study medication, we will ask you to record any other medications that your baby is taking. We will draw blood to monitor your baby's reaction to the medication. We will also draw blood to measure the level of medication in your baby's body. We will also draw some blood, swab your baby's mouth and collect a urine sample to determine the |

| | |
|---|---|
| | amount of virus in your baby's body at these visits. See the Study Participation and Procedures section for more details. |
| **Risks** | The most common reported side effects reported with Letermovir (study medication) are nausea, diarrhea, vomiting, cough, swelling in the hands and feet, feeling tired, headache and stomach pain. The risk with blood drawing is bruising where the blood is collected and discomfort. An infection (rare) or a small clot may also occur at the site of the blood draw. A risk of putting a urine bag on your baby to collect the urine sample is redness or skin irritation. A breach of confidentiality is another risk. See the Risks and Discomforts section for more details on the risks. |
| **Benefits** | There is no benefit for participating in this study. Information gathered from this study may help doctors take care of babies exposed to CMV during the birthing process in the future. |
| **Alternatives** | The alternative to participation in the study is to have your clinical doctor treat your baby for CMV with standard of care treatment. |

## Purpose of the Research

The purpose of this study is to determine the dose of a new medication being studied for babies who are exposed to cytomegalovirus during birth. This is called congenital cytomegalovirus (cCMV). Cytomegalovirus is the leading cause of hearing loss and the leading viral cause of developmental delays in children. If your baby participates in this study, in addition to the study medication, he/she will still receive the current best treatment for cCMV, which is oral Valganciclovir.

Your baby's doctor has determined that your baby has congenital cytomegalovirus (cCMV). cCMV is where your baby is born with cytomegalovirus (CMV). Letermovir is the first newly licensed medication with activity against CMV in over 20 years but has not yet been approved by the Food and Drug Administration (FDA) for use in babies. The current treatment for cCMV is to use Valganciclovir by mouth. This medication has been shown in earlier studies to be somewhat effective in preventing hearing loss or hearing deterioration in babies with symptomatic CMV disease, but does not provide full hearing protection in all babies. The combination of these two medications (Letermovir and Valganciclovir) with different methods of actions may enhance the benefits on both hearing and development. The purpose for this study is to determine the dose of medication (Letermovir) needed to treat babies diagnosed with cCMV. The new medication, Letermovir, is investigational.

This study will enroll 8 participants at multiple research sites in the US. We will enroll approximately XX participants at Site Name. Please read this information and feel free to ask any questions before you agree to allow your baby to take part in the study. Your baby's participation is voluntary. You may refuse to allow your baby to participate in this study, and you may remove your baby from the study at any time.

## Study Participation and Procedures

The study team will see your baby in clinic on Study Visits, 1, 5, 10, 14, 21 and 42. You will bring your baby to the clinic to receive their study medication or someone from the study team will watch you mix and administer the medication in person or on video on Study Visits 2, 3, 4, 6, 7, 8, 9, 11, 12, and 13.

**Study Day 1 (4 hours)** – This is the day that you sign the consent agreement to participate in the study.

- We will collect some basic information about your baby such as date of birth, race, sex, birth weight, weight at enrollment, length at enrollment, estimated age at time of delivery and medical conditions that your baby had prior to being in the study.
- Your baby will have a small amount of blood (2.2ml or 1/2 teaspoon) taken to determine the amount of study medication, Valganciclovir (medication prescribed by your baby's doctor) medication, and cytomegalovirus in their blood. We will monitor your baby's kidneys and cells that fight off infection.
- Your baby will receive their first dose of the study medication (Letermovir) in their formula based on how much they weigh on Study Day 1. Your baby will start taking the new study medication dose once a day by mouth for the next 14 days (Days 1-14). If your baby misses a dose, vomits, or spits up the medication, it will not be repeated.
- Your baby will also start taking Valganciclovir at a dose determined by their clinical care doctor.
- We will check to see if your baby is having any issues from taking the medication.
- We will record any medications that your baby is taking.
- We will collect a small amount of urine and swab your baby's mouth to determine the amount of virus that is in their body.

**Study Days 2, 3 and 4 (30 minutes)**

- You will bring your baby to the clinic to receive his or her study medication or someone from the study team will watch you mix and administer the medication in person or on video.
- We will ask you to record any medications that your baby is taking.

**Study Days 5 and 14 (2 hours)**

- Your baby will have a small amount of blood (2.2ml or 1/2 teaspoon) taken to determine the amount of study medication, Valganciclovir (medication prescribed by your baby's doctor) medication, and cytomegalovirus in their blood. We will monitor your baby's kidneys and cells that fight off infection.
- We will check to see if your baby is having any issues from taking the medication.
- We will ask you to record any medications that your baby is taking.
- We will collect a small amount of urine and swab your baby's mouth to determine the amount of virus that is in their body.

**Study Days 6, 7, 8 and 9 (30 minutes)**

- You will bring your baby to the clinic to receive his or her study medication or someone from the study team will watch you mix and administer the medication in person or on video.
- We will ask you to record any medications that your baby is taking.

**Study Day 10 (24 hours)**

- Your baby will have a small amount of blood (0.2mL or 1/25 teaspoon) taken 5 different times over a 24 hour period to determine the amount of study medication in your baby's blood. We will use some of this blood to determine the amount of Valganciclovir (medication prescribed by your baby's doctor) that is in your baby's blood.
- Your baby will also have a small amount of blood (2.2ml or 1/2 teaspoon) taken to determine the amount of study medication, Valganciclovir (medication prescribed by your baby's doctor) medication, and cytomegalovirus in their blood. We will monitor your baby's kidneys and cells that fight off infection.
- We will check to see if your baby is having any issues from taking the medication.

- We will ask you to record any medications that your baby is taking.
- We will collect a small amount of urine and swab your baby's mouth to determine the amount of virus that is in their body.

**Study Days 11, 12 and 13 (30 minutes)**

- You will bring your baby to the clinic to receive his or her study medication or someone from the study team will watch you mix and administer the medication in person or on video.
- We will ask you to record any medications that your baby is taking.

**Study Days 21 and 42 (1 hour)**

- Your baby will have a small amount of blood (0.5ml or 1/10 teaspoon) taken to determine the amount of cytomegalovirus in their blood.
- We will check to see if your baby is having any issues from taking the medication.
- We will collect a small amount of urine and swab your baby's mouth to determine the amount of virus that is in their body.

Letermovir that is administered by mouth will be supplied by the study. Your baby's clinical care doctor will determine the dose and amount of time that your baby will be on Valganciclovir. Valganciclovir will not be provided by the study. If your baby misses a dose of the study medication, it will be recorded in the study records. The number of days will not be extended to allow your baby to make up the missed dose.

Your baby may begin the study while they are still in the hospital. We will complete your baby's study visits while they are in the hospital.

The study doctor will discuss with you your responsibilities as a participant. The table below shows the study days and what will be done on each day.

| | **Study Day (window)** | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 5 (± 2 days) | 10 (± 2 days) | 14 (± 1 day) | 21 (± 2 days) | 42 (+ 7 days) |
| Blood drawn | X | X | X | X | X | X |
| Study Medication Side Effect Check | X | X | X | X | X | X |
| Urine collected | X | X | X | X | | |
| Mouth swab collected | X | X | X | X | X | X |
| Letermovir (study medication) | ← | — | → | | | |
| Valganciclovir (Prescribed by your doctor) | ← | — | → | | | |
| Total amount of blood required | ½ tsp | ½ tsp | ⅔ tsp | ½ tsp | 1/10 tsp | 1/10 tsp |

**Additional Information:**
Your de-identified private information and de-identified biospecimens (private information and biospecimens with all identifiers removed) may be used for future research studies or distributed to another researcher for future research studies without additional informed consent. **This is only when there are no identifiers associated with the data or biospecimens.**

The clinical results (including individual research results) may be returned to you or your baby's doctor if requested to help your baby's doctor to better care for your baby.

## Risks and Discomforts

There may also be risks that are unknown at this time. You will be given more information if other risks are found.

***Study Medication***

Letermovir has been shown to have a good safety profile. The most common reported side effects are nausea, diarrhea, vomiting, swelling in the hands and feet, cough, headache, feeling tired and pain in the stomach. We will ask that you keep a log of any side effects that your baby has while on the study and to notify the study staff of any concerns that you have.

***Blood draw:***

There may be discomfort from the needle stick and occasional bruising at the site during or after the blood drawing and rarely an infection. A small clot may form at the site where the needle enters the body. Some people faint when having their blood drawn. All blood draws will be done using sterile techniques.

***Urine Collection:***

Your baby may have a small bag placed over their genitals to collect a urine sample. This should not be uncomfortable for your baby. The tape on the bag may cause your baby's skin to turn red.

***Risks of Loss of Confidentiality from Storage and Sharing of Samples and Data***

When we store your baby's data and samples, we take precautions to protect your baby's information from others that should not have access to it. When we share your baby's data and samples, we will do everything we can to protect your baby's identity by removing information that can identify them. Even with the safeguards we put in place, we cannot guarantee that your baby's identity will never become known or someone may gain unauthorized access to your baby's information. New methods may be created in the future that could make it possible to re-identify your baby's data or samples.

## Benefits

There is no direct benefit to your baby for participating in this study. The current treatment for cCMV is to use Valganciclovir by mouth. This medication has been shown in earlier studies to be effective in preventing hearing loss or hearing deterioration in babies with symptomatic CMV disease. The combination of these two medications (Letermovir and Valganciclovir) with different methods of actions may enhance the benefits on both hearing and development. The current study will give us information

about what dose of Letermovir to use in babies. Information gathered from this study may help doctors take care of babies exposed to cCMV in the future.

## Alternatives

The alternative is to not participate in this study. The study doctor will discuss with you the alternatives to participation and their risks and benefits.

## Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Insert Site Confidentiality and HIPAA Authorization Language

Merck, the maker of the study drug is a collaborator on this study. They will have access to your baby's protected health information through monitoring the study sites.

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

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify your baby in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your baby's medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about your baby's involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

## Voluntary Participation and Withdrawal

Whether or not you allow your baby to take part in this study is your choice. There will be no penalty if you decide to withdraw your baby from the study. If you decide not to allow your baby to be in the study, your baby will not lose any benefits your baby is otherwise owed.

You are free to withdraw your baby from this study at any time. Your choice to have your baby leave the study will not affect your baby's relationship with this institution. However, your baby should return to see the study doctor for safety reasons so your baby can be taken off the study medication and referred for follow-up care. Contact the study doctor if you want to withdraw your baby from the study.

Your baby may be removed from the study without your consent if the sponsor ends the study, if the study medication is approved by the FDA, if the study doctor decides it is not in the best interest of your baby's health, or if you are not following the study rules.

**Cost of Participation**

There will be no cost to your baby for taking part in this study. All exams and tests related to this study will be provided to your baby at no cost during the 42-day study period. The costs of your baby's standard medical care will be billed to your baby and/or your baby's insurance company in the usual manner.

**Payment for Participation in Research**

Insert Site Language

**Payment for Research-Related Injuries**

Insert Site Language

**New Findings**

You will be told by the study doctor or the study staff if any new information becomes available that might affect your willingness to allow your baby to stay in the study.

**Questions**

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the research doctor**.** Your baby's doctor will be glad to answer any of your questions. Site PI Name may be reached at Site PI Contact Telephone Number(s).

Insert Site IRB/HRPP Contact Information

This study is being conducted in collaboration with the University of Alabama at Birmingham (UAB). If you have questions about your baby's rights as a research participant, or concerns or complaints about the research, you may also contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

**Optional**

**Future Research Use of Identifiable Information and Biospecimens**

We would like your permission to keep your baby's private information (data containing personal information) and biospecimens (blood, saliva and urine) collected in this study for future research. The

future research may be similar to this study or may be completely different. These studies may be done by researchers at this institution or other institutions, including commercial entities. Our goal is to make more research possible. Your baby's private information and biospecimens will be stored indefinitely or until used.

Your baby's private information and biospecimens will be identifiable. Results of any future research will not be given to you or your baby's doctor

Your baby can take part in this study even if you decide not to let us keep your baby's research information and biospecimens for future research.

If you give us permission now to keep your baby's research information and biospecimens, you can change your mind later and ask us to destroy it. However, once we have analyzed your baby's private information and biospecimens, we may not be able to take it out of our future research.

We may share your baby's research information and biospecimens, so that others can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your baby's research information and biospecimens with other researchers, we will not be able to get it back.

Future research use of your baby's research information and biospecimens will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of the future research. Allowing us to do future research on your baby's research information and biospecimens will not benefit you or your baby directly.

The research information and biospecimens used for future research may be used for commercial profit. There are no plans to provide financial compensation to you or your baby should this occur.

This research is part of the Rare Diseases Clinical Research Network (RDCRN), an initiative of the National Institutes of Health (NIH) to advance medical research on rare diseases. A long-term goal of the network is to improve diagnosis and treatment of rare disease conditions. The clinical information collected for this study will be stored at the NIH-funded RDCRN Data Management and Coordinating Center and also will be also part of a Federal data repository hosted by the NIH. The NIH and the data management center uses several layers of protection for the clinical data stored there. It meets all of the local and federal security requirements for research datacenters. The NIH may make your data, without direct personal identifiers, available for other research studies in the future. Future research may be about similar diseases or conditions to this study, but could also be about unrelated diseases, conditions, or other aspects of health. Researchers who want access to your data will have to tell the NIH, through a data access request and application process, about the research they want to do. They will have to do ethics training and have IRB approval to do the research. They will have to sign a legal agreement stating they will not try to find out who you are.

**Initial your choice below:**

___ I agree to allow my baby's research information and biospecimens to be kept and used for future research.

___ I do not agree to allow my baby's research information and biospecimens to be kept and used for future research.

If, in the future, you decide that you do not want your baby's research information and biospecimens used for research, please notify Site PI Name or the study team at Site Contact Telephone Number and your baby's specimens will be destroyed once all study test are completed.

**Legal Rights**

You are not waiving any of your baby's legal rights by signing this consent form.

**Signatures**

You are making a decision whether or not to allow your baby to participate in this study. Your signature indicates that you have read (or have been read) the information provided above and decided to allow your baby to participate. You will receive a copy of this signed consent form.

| Signature of Parent or Guardian | Date | Time |
|---|---|---|

| Signature of Parent or Guardian | Date | Time |
|---|---|---|

☐ Check here if only one parent/guardian is reasonably available to provide consent and provide a reason:_____

_____

| Signature of Person Obtaining Consent | Date | Time |
|---|---|---|