

# Study on children treated for CMV infection at birth

<b>Submission date</b> 20/12/2024	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 24/02/2025	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 11/04/2025	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Congenital cytomegalovirus (cCMV) is a rare infection. It happens when the CMV transfers from the mother to the baby during pregnancy. It is a significant cause of hearing loss in newborns and children up to 4 years old. cCMV is also the most frequently known viral cause of general learning disability in children. Some children with cCMV are treated with a specific type of medication called an 'antiviral'. This study is looking at the long-term effects of two antiviral medications, Ganciclovir and Valganciclovir. We want to look at the impact these medicines have had on patients' hearing and overall neurological and physical development over time, as well as studying the long-term safety profile of these drugs. This is a natural history study. This means that we will not provide treatment for cCMV in this study.

### Who can participate?

Children  $\geq 2$  years old to  $<16$  years old who were previously treated with intravenous ganciclovir or oral valganciclovir for congenital CMV infection at sites participating in the Collaborative Antiviral Study Group.

### What does the study involve?

This study involves asking questions about their medical history, collecting some information from their medical records, performing a physical exam, and carrying out some tests. We will perform some tests that will look at their memory, speech, problem-solving, motor skills, and listening skills (neurodevelopment assessment). We will test their hearing (hearing assessment). We will collect some urine, saliva, and blood. We will take a picture (x-ray) of their left wrist to look at the age of the bone.

### What are the possible benefits and risks of participating?

**Benefits:** there may be no direct benefit from participating in this study. The results from this study may help guide research into the treatment of congenital CMV in the future.

### Risks:

- Physical exam: this includes an assessment of their breasts (for girls) and genitals, which may make them feel uncomfortable.
- Saliva swab: this may be uncomfortable but there are no associated risks with this procedure.

- Blood sample collection: there may be discomfort from the needle stick and occasional bruising at the site during or after the blood draw, and rarely, an infection.
- Wrist X-ray: the wrist X-ray will expose your child to low amounts of radiation. This is for research purposes and you would not receive this radiation if they were not part of this study. Every day, people are exposed to low levels of radiation. This radiation comes from the natural environment and man-made radiation sources around them. This type of radiation is called "background radiation." The typical radiation dose from a wrist radiograph is 0.001mSv. This is the same amount of radiation you receive from the natural background of the Earth in less than 3 hours. The probability of harm from participating in this study is low compared to other everyday risks. Certain diseases or conditions may affect sensitivity to radiation. We will not ask your child to have an x-ray if they are pregnant.

Where is the study run from?

Approved research sites in the UK

When is the study starting and how long is it expected to run for?

October 2024 to April 2025.

Who is funding the study?

The National Institutes of Health (NIH), USA, from the University of Alabama in Birmingham (UAB) USA

Who is the main contact?

Dr Simon Drysdale (Chief Investigator UK), [childrensresearch@paediatrics.ox.ac.uk](mailto:childrensresearch@paediatrics.ox.ac.uk)

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Dr Simon Drysdale

### ORCID ID

<https://orcid.org/0000-0002-6350-6557>

### Contact details

Children's Research Office  
Department of Paediatrics  
University of Oxford  
Lower Ground 1 Door LG1-10-15  
Children's Hospital at John Radcliffe Hospital Site  
Headley Way  
Headington  
Oxford  
United Kingdom  
OX3 9DU  
+44 (0)1865 2 27503  
[childrensresearch@paediatrics.ox.ac.uk](mailto:childrensresearch@paediatrics.ox.ac.uk)

# Additional identifiers

## Clinical Trials Information System (CTIS)

Nil known

## Integrated Research Application System (IRAS)

341389

## Protocol serial number

PID 18211, DMID 22-0013, NIH funding mechanism 1U54AI150225, CPMS 62464

# Study information

## Scientific Title

A retrospective follow-up study of the durability of antiviral therapy on long-term hearing and neurodevelopmental outcomes among patients treated for congenital cytomegalovirus infection as infants or toddlers

## Acronym

cCMV Retrospective Follow-up Study

## Study objectives

This study is looking at the long-term effects of two antiviral medications, ganciclovir and valganciclovir. We want to look at the impact these medicines have had on patients' hearing and overall neurological and physical development over time, as well as studying the long-term safety profile of these drugs.

This is a natural history study. This means that we will not provide treatment for cCMV in this study.

## Ethics approval required

Ethics approval required

## Ethics approval(s)

approved 21/11/2024, Health and Social Care Research Ethics Committee B (HSC REC B) (Business Services Organisation (BSO) Headquarters, 2 Franklin Street, Belfast, BT2 8DQ, United Kingdom; +44 (0)28 9536 1400; RECB@hscni.net), ref: 24/NI/0136

## Study design

Natural history study

## Primary study design

Observational

## Study type(s)

Other, Safety

## Health condition(s) or problem(s) studied

Congenital cytomegalovirus (CMV) infection

## Interventions

Participants enrolling in this retrospective follow-up study will have audiologic and neurodevelopmental assessments obtained, as well as assessments for long-term endocrine (pubertal) and oncologic toxicities of valganciclovir therapy early in life. They also will have virologic and immunologic testing to determine changes in both the virus and host over years following antiviral therapy.

## **Intervention Type**

Other

## **Primary outcome(s)**

Change in total ear hearing assessments since completion of antiviral therapy, adjusted for age at initiation of therapy and time since completion of therapy. This is measured through a hearing assessment on a single study visit.

## **Key secondary outcome(s)**

1. Change in best ear hearing assessments since completion of antiviral therapy, adjusted for age at initiation of therapy and time since completion of therapy. This is measured through a hearing assessment (either, traditional, play, Visual Reinforcement Audiometry, or otoacoustic emission testing and/or auditory brainstem response) on a single study visit.
2. Neurodevelopmental assessment at the time of the single study visit. This is a measure through neurodevelopment assessment (tailored to participants' abilities and age: either WPPSI-IVUK, WISC-VUK, Leither-3, or Bayley-4) on a single study visit.
3. Any development of cancer before the single study visit. This data is collected from the participant as medical history on a single study visit.
4. Pubertal development (delayed, age-appropriate, advanced) at the time of the single study visit. This data is collected from the participant as medical history and physical exam on a single study visit.

Exploratory endpoints:

1. Cell-mediated immunity against CMV. This is measured on a blood sample (T-SPOT.CMV assay) at the time of the single study visit.
2. CMV genotypes. This is measured from blood, urine, and saliva samples (viral load by PCR) at the time of the single study visit.
3. Ganciclovir resistance mutations in CMV-positive blood, urine, and saliva samples at the time of the single study visit (if the viral load is sufficiently elevated by Next Generation Sequencing).

## **Completion date**

31/03/2025

## **Eligibility**

### **Key inclusion criteria**

1. Signed informed consent from the participant, the parent(s) or legal guardian(s), with signed assent from the participant (as appropriate)
2.  $\geq 2$  years old to  $< 16$  years old
3. One of the following:
  - 3.1. Prior receipt of intravenous ganciclovir or oral valganciclovir for the clinical treatment of congenital CMV infection by clinicians at a current or former CASG study siteOR
  - 3.2. Prior receipt of intravenous ganciclovir or oral valganciclovir through participation in a CASG study of the treatment of congenital CMV

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Child

**Lower age limit**

2 years

**Upper age limit**

16 years

**Sex**

All

**Total final enrolment**

5

**Key exclusion criteria**

Unable to comply with study-related procedures

**Date of first enrolment**

02/01/2025

**Date of final enrolment**

31/03/2025

**Locations****Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Oxford University Hospitals NHS Foundation Trust**

Children's Research Office

Lower Ground 1, Door LG1-10-15

Headley Way

Headington

Oxford

United Kingdom

OX39DU

**Study participating centre****The Newcastle upon Tyne Hospitals NHS Foundation Trust**

Royal Victoria Infirmary

Queen Victoria Road

Newcastle upon Tyne

United Kingdom

NE1 4LP

**Study participating centre****Great Ormond Street Hospital for Children NHS Foundation Trust**

Great Ormond Street

London

United Kingdom

WC1N 3JH

**Study participating centre****St George's University Hospitals NHS Foundation Trust**

St Georges Hospital

Cranmer Terrace

London

United Kingdom

SW17 0RE

**Sponsor information****Organisation**

University of Oxford

**ROR**<https://ror.org/052gg0110>**Funder(s)****Funder type**

Government

**Funder Name**

University of Alabama at Birmingham USA (through NIH)

**Alternative Name(s)**

The University of Alabama at Birmingham, U. of Alabama at Birmingham, University of Alabama - Birmingham, Medical College of Alabama, Birmingham Extension Center, College of General Studies, The University of Alabama in Birmingham, University of Alabama in Birmingham, UAB

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Universities (academic only)

**Location**

United States of America

**Funder Name**

National Institutes of Health

**Alternative Name(s)**

US National Institutes of Health, Institutos Nacionales de la Salud, NIH, USNIH

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United States of America

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are not expected to be made available due to data protection regulations.

**IPD sharing plan summary**

Not expected to be made available