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Study on children treated for CMV infection at birth

Submission date 20/12/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 24/02/2025	**Overall study status** Completed	
Last Edited 11/04/2025	**Condition category** Infections and Infestations	

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 ≥ 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

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
341389

Central Portfolio Management System (CPMS)
62464

Protocol serial number
PID 18211, DMID 22-0013, NIH funding mechanism 1U54AI150225

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. ≥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 site
OR
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
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Study participating centre
Great Ormond Street Hospital for Children NHS Foundation Trust
Great Ormond Street
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Study participating centre
St George's University Hospitals NHS Foundation Trust
St Georges Hospital
Cranmer Terrace
London
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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