ISRCTN80374799 https://doi.org/10.1186/ISRCTN80374799

Does treating cytomegalovirus and tuberculosis very early (even without being sure if the child has these infections) in addition to the usual treatment for pneumonia save HIV-positive children's movement and reasoning?

Submission date
10/12/2021

Recruitment status
No longer recruiting

Registration date
17/01/2022

Overall study status
Completed

Last Edited
27/08/2024

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Human Immunodeficiency Virus (HIV) infection remains a major threat to the lives of many children in Sub-Saharan Africa. Despite the great strides towards the reduction of HIV-associated mortality, and improved survival of children infected with HIV, their quality of life remains a major priority. Infections like HIV and severe pneumonia increase the risk of developing significant motor (movement) and cognitive (reasoning) deficits.

The EMPIRICAL study aims to find out if giving treatment for cytomegalovirus and tuberculosis very early (even without being sure if the child has these infections) in addition to the usual treatment for pneumonia in children with HIV, is better for a child than receiving only the treatment for pneumonia.

This study aims to find out if this treatment could also save children's movement and reasoning. This study will compare movement and reasoning scores of children participating in the EMPIRICAL trial who received the additional treatment to those who did not. The study will also compare the scores of children who received additional treatment to those who have HIV but no pneumonia and to those who have no HIV but have pneumonia.

Who can participate?
Caregivers of children who are either participating in the EMPIRICAL trial (HIV-infected with severe pneumonia), HIV positive children without pneumonia, or HIV negative children with pneumonia, and are aged between 28 and 1 year in Uganda will be asked to participate.

What does the study involve?
A pre-tested questionnaire will be used to collect information from caregivers about their child's birth, circumstances around their child's growth, information about the child's main caretaker,

and family's wellbeing. The study will then measure the child's movement, thinking, and reasoning abilities by interacting with the child. Children participating in the study will be followed up for 2 years, initially at discharge from hospital, at 1 year, and after 2 years.

What are the possible benefits and risks of participating?
Caregivers might feel uncomfortable with spending more time in the hospital while their child is being assessed. If their child is found to have any problems with their movement, thinking, or reasoning to levels that need treatment, caregivers will be given an opportunity to decide if they would like to be told these findings. This study will not expose the child to any other risk.

Caregivers will get a chance to know about their child's performance on these tests. If the child is found to have any problems with their movement, thinking, or reasoning to levels that need treatment, caregivers will be advised on the treatment required and referred to specialists in this area. From this study, we may learn more about the thinking/reasoning and movement of HIV-infected children with severe pneumonia. All of these findings may one day help us to better treat other children with HIV and severe pneumonia.

The records of this study will be kept private. The only people with access to the personal information of the caregiver or child will be the employees of the hospital where the child is being looked after. The child's name will not appear in any information published about this study. Personal pseudo-anonymized information will be accessed by the study team members, and the Ethics Committees but always without the name of the child. Any study data that is to be transmitted via the Internet will be encrypted with secure passwords known to the sender and recipient(s) only. The child's confidentiality will be protected to the maximum extent allowable by law. Participants in the study have the right to access, rectify or erase their personal data; restrict the types of activities the research team can do with their personal data; object to using their personal data for specific types of activities, or withdraw their consent.

Where is the study run from?
Makerere University (Uganda)

When is the study starting and how long is it expected to run for?
From December 2020 to April 2025

Who is funding the study?
European & Developing Countries Clinical Trials Partnership (EDCTP)

Who is the main contact?
Dr Damalie Nalwanga
damalielwanga@gmail.com

Contact information

Type(s)
Public

Contact name
Dr Damalie Nalwanga

ORCID ID
https://orcid.org/0000-0002-1862-8109

Contact details
Makerere University
Kampala
Uganda
256
+256 (0)414699134
damalielwanga@gmail.com

Additional identifiers

Protocol serial number
TMA2020CDF-3198

Study information

Scientific Title
Neurocognitive function among HIV-infected infants with severe pneumonia receiving empirical treatment for cytomegalovirus and tuberculosis

Acronym
Neuro-Empirical

Study objectives
Because empirical treatment for CMV and TB among HIV positive children with severe pneumonia would reduce duration of hospitalization and risk of complications, it is expected to produce better neurocognitive outcomes at 2 years of follow up compared to those receiving standard of care alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/05/2021, School of Medicine Research Ethics Committee (P.O. Box 7072 Kampala, Uganda; +256 414 533541; rresearch@gmail.com), ref: 2019-115

Primary study design
Observational

Study design
Prospective longitudinal observational study of a cohort nested under the EMPIRICAL study (a randomized open-label clinical trial) in comparison to two separate longitudinal cohorts

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neurocognitive function among HIV-infected children hospitalized with severe pneumonia

Interventions

This study is a prospective longitudinal observational study nested under the EMPIRICAL study (a randomized open-label clinical trial) compared to a longitudinal cohort of HIV-negative children with severe pneumonia, as well as a cross-sectional cohort of HIV-positive children without pneumonia.

Eligible participants will be identified and approached during hospitalization. Eligible participants who give informed consent will be consecutively enrolled in the study. A pre-tested questionnaire will be used to collect participants' baseline data including age, sex, a detailed anthropometric assessment (weight, length, weight for length z score and head circumference), duration on ART for those who will have already started ART, ART exposure in utero, treatment adherence using 3-day recall, history of prematurity, prior hospitalization and laboratory findings including hemoglobin, CMV viral load, HIV viral load, and CD4 cell count. Other independent variables will include birth history (birth weight and history of requiring resuscitation), caretaker data (relationship with the child, level of education, depression score), and family socioeconomic status.

At 1-year post-randomization and 2 years of age, a follow-up questionnaire will be applied evaluating caretaker data, socioeconomic status, and anthropometric measurements. Neurodevelopmental assessments will be done at baseline (at discharge from hospital since they will be stable enough to do the neurocognitive tests), at 1 year post-randomization to receive the assigned intervention (empirical treatment for CMV, TB, or both i.e. cases) or no intervention (controls) to establish the trend of neurocognitive function, and at 2 years of age.

Intervention Type
Other

Primary outcome(s)
Development measured in participants the intervention group (empirical treatment for CMV, TB, or both) and SoC alone using mean scaled scores on the Bayley scale of infant development at discharge, 1 year post-randomization, and at 2 years of age

Key secondary outcome(s)
1. Development measured in participants the intervention group (empirical treatment for CMV, TB, or both), SoC alone, and a matched cohort of HIV-positive infants without pneumonia using mean scaled scores on the Bayley scale of infant development at discharge, 1-year post-randomization, and at 2 years of age
2. Development measured in participants the intervention group (empirical treatment for CMV, TB, or both), SoC alone, and a cohort of HIV negative infants with severe pneumonia using mean scaled scores on the Bayley scale of infant development at discharge, 1 year post-randomization, and at 2 years of age

Completion date
30/04/2025

Eligibility

Key inclusion criteria
Cohort of HIV positive children with severe pneumonia:
1. Aged between 28 and 365 days
2. Participating in the EMPIRICAL trial
3. Current hospitalization due to pneumonia with criteria for parenteral antibiotics (≥1 World

Health Organization criteria)
4. Pneumonia, defined as chest indrawing or fast breathing for age (for infants aged 28 to 60 days, ≥60 breaths per minute; for infants aged 61 to 365 days, ≥50 breaths per minute)
5. HIV-confirmed infection (with at least one molecular method: DNA PCR or RNA PCR/viral load)
6. Informed consent obtained from caregivers

Cohort of HIV negative children with severe pneumonia:
1. Aged between 28 and 365 days
2. Current hospitalization due to pneumonia with criteria for parenteral antibiotics (≥1 World Health Organization criteria)
3. Pneumonia, defined as chest indrawing or fast breathing for age (for infants aged 28 to 60 days, ≥60 breaths per minute; for infants aged 61 to 365 days, ≥50 breaths per minute)
4. Informed consent obtained from caregivers

Cohort of HIV positive children without pneumonia:
1. Aged between 28 and 365 days
2. HIV-confirmed infection (with at least one molecular method: DNA PCR or RNA PCR/viral load)
3. Informed consent obtained from caregivers

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
28 Days

Upper age limit
365 Days

Sex
All

Total final enrolment
105

Key exclusion criteria
1. Clinical TB (pulmonary or extrapulmonary) diagnosis. Defined as the necessity of TB treatment prescribed by a physician, known bacteriologically confirmed TB case (at least one biological specimen positive by culture or Xpert MTB/RIF) at the moment of randomization, previously treated for TB or currently on treatment for TB, or documented evidence of close TB exposure.
2. Pure wheezers. Defined as a clear clinical improvement after a bronchodilator test.
3. Active malignancies, systemic immunosuppressive medications, or evidence of condition other than HIV and pneumonia
4. Weighing <2.5 kg
5. Hemoglobin less than <6 g/dl in the screening blood test or in a test done in the last 48 h
6. Neutropenia <500 /mm^3 in the screening blood test or in a test done in the last 48 h

Date of first enrolment
05/05/2021

Date of final enrolment
08/09/2023

Locations

Countries of recruitment
Uganda

Study participating centre
Makerere University
P.O Box 7072
Kampala
Uganda
256

Sponsor information

Organisation
Makerere University

ROR
https://ror.org/03dmz0111

Funder(s)

Funder type
Government

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
The European & Developing Countries Clinical Trials Partnership, The European & Developing Countries Clinical Trials Partnership (EDCTP), European and Developing Countries Clinical Trials, Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, EDCTP

Funding Body Type

Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available on request. Anyone interested in accessing the de-identified patient datasets can reach out on the contact email address provided and the study contact will respond to the request accordingly

IPD sharing plan summary
Available on request