

Assessment of the ability of artemether-lumefantrine and dihydroartemisinin – piperazine to treat simple malaria in children in Uganda

Submission date 17/08/2015	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 20/10/2015	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 14/01/2020	Condition category Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Malaria is a serious infectious disease which is common in tropical and subtropical countries. It is caused by a microscopic parasite which is spread from person to person by mosquitos. There are a lot of different drugs which are used to treat malaria, which are often used in combination with each other. The aim of this study is to compare the success of two different drug combinations (the drug combination dihydroartemisinin-piperazine (AP), and the drug combination artemether-lumefantrine (AL) when treating malaria in young children.

Who can participate?

Children suffering from fever living within the catchment areas of the trial centres

What does the study involve?

The children involved in the study are randomly split into two groups. The first group is treated with AP and the second group is treated with AL. For the first three days after the treatment, the children's temperature is measured to check for signs of a fever. Blood samples are taken from the children on days 1, 2, 3, 7, 14, 21, 28, 35 and 42 so the success of the drugs can be found out by looking at the levels of the parasites and how many of different types of blood cells are in the blood.

What are the possible benefits and risks of participating?

Potential benefits for participants include the good quality care that they receive from medical officers and nurses while taking part in the study. There are no direct risks of participating in the study, other than known or unknown side effects of the medications being provided.

Where is the study run from?

1. Aura Hospital (Uganda)
2. Mbarara Hospital (Uganda)
3. Nagongera Health Centre IV (Uganda)

When is the study starting and how long is it expected to run for?
September 2015 to September 2017

Who is funding the study?
1. Ministry of Health (Uganda)
2. The World Bank (USA)

Who is the main contact?
Dr Adoke Yeka
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Protocol version 1.2

Study information

Scientific Title
Efficacy of artemether-lumefantrine and dihydroartemisinin – piperaquine for treatment of uncomplicated malaria in children in Uganda

Study objectives
The risk of treatment failure unadjusted by genotyping will be lower in the dihydroartemisinin–piperaquine arm compared to the artemether-lumefantrine arm at each of the sites.

Ethics approval required

Old ethics approval format

Ethics approval(s)

1. Makerere University School of Public Health Research Higher Degrees Research and Ethics Committee, 10/06/2015, ref: 205
2. Uganda National Council of Science and Technology, 26/06/2015, ref: HS 1356

Study design

Multi-centre single-blinded randomised parallel trial.

Primary study design

Interventional

Secondary study design

Randomised parallel trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Malaria

Interventions

Subjects who meet the selection criteria will be randomized to treatment with artemether-lumefantrine (AL) or dihydroartemisinin-piperaquine (DP) and will be followed for 42 days. Repeat evaluations will be performed on days 1, 2, 3, 7, 14, 21, 28, 35 and 42 (and any unscheduled days) and will include assessment for the occurrence of adverse events.

Intervention Type

Drug

Phase

Phase IV

Drug/device/biological/vaccine name(s)

1. Dihydroartemisinin-piperaquine
2. Artemether-lumefantrine

Primary outcome measure

1. Risk of parasitological treatment failure (Early Treatment Failure (ETF)
2. Late Parasitological Failure (LPF)
3. Late Clinical Failure (LCF))

All assessed after 42 days of follow-up unadjusted and adjusted by genotyping to distinguish recrudescence from new infections. Risks will be estimated using the Kaplan-Meier product limit formula based on a modified intention-to-treat analysis.

Secondary outcome measures

1. Prevalence of fever (defined as both subjective fever in the previous 24 hours and measured axillary temperature greater than 37.5°C) on follow-up days 1, 2, and 3
2. Prevalence of parasitemia (proportion of patients with malaria parasites in their blood) on follow-up days 1, 2 and 3
3. Parasite clearance time. Defined as the number (n) and the proportion (%) of patients with a positive parasite count on day 2 and 3 as well as the number (N) of patients evaluated on that day shall be estimated. The parasite clearance rate and initial parasite clearance lag phase duration shall be estimated by modelling the log (parasitemia) time profile using the PCT calculator
4. Change in mean hemoglobin from day 0 to 42 (or day of rescue therapy for patients classified as LCF or LPF), measured from blood samples
5. Prevalence of gametocytemia and gametocyte density in the blood on follow-up days 1, 2, 3, 7, 14, 21, 28, 35 and 42
6. Proportion of patients experiencing any serious adverse event in each treatment group during the 42-day follow-up period (both including and excluding patients classified as ETF or LCF, as recurrent malaria can be confounding)
7. Proportion of patients with adverse events of moderate or greater severity, at least possibly related to the study medications, excluding patients requiring quinine therapy during follow up days.
8. Change in the prevalence of molecular markers in the blood, associated with drug resistance (proportion of patients who fail treatment with K 13 mutants) from day 0 to the day of recurrent parasitemia

Overall study start date

01/09/2015

Completion date

01/09/2017

Eligibility

Key inclusion criteria

1. Age 6 – 59 months
2. Fever (> 37.5°C axillary) or history of fever in the previous 24 hours
3. Ability to participate in 42-day follow-up (patient has easy access to health unit)

Participant type(s)

Patient

Age group

Child

Lower age limit

6 Months

Upper age limit

59 Months

Sex

Both

Target number of participants

600

Total final enrolment

599

Key exclusion criteria

1. Weight < 5 kg
2. History of serious side effects to study medications
3. Concomitant febrile illness or presence of intercurrent illness or any condition (cardiac, renal, hepatic diseases) which would place the subject at undue risk or interfere with the results of the study
4. Treatment with antimalarial drugs (ACTs) already started and ongoing prophylaxis with drugs having antimalarial activity such as cotrimoxazole for the prevention of Pneumocystis carinii pneumonia in children born to HIV+ women.
5. Severe malnutrition (defined as weight for height <70% of the median NCHS/WHO reference)
6. Danger signs or evidence of severe malaria:
 - 6.1. Unarousable coma (if after convulsion, > 30 min)
 - 6.2. Recent convulsions (1-2 within 24 h)
 - 6.3. Altered consciousness (confusion, delirium, psychosis, coma)
 - 6.4. Lethargy
 - 6.5. Unable to drink or breast feed
 - 6.6. Vomiting everything
 - 6.7. Unable to stand/sit due to weakness
 - 6.8. Severe anemia (Hb < 5.0 gm/dL)
 - 6.9. Respiratory distress (labored breathing at rest)
 - 6.10. Jaundice
7. Severe malnutrition (defined as a child whose growth standard is below -3 z-score, has symmetrical oedema involving at least the feet or has a mid-upper arm circumference < 110 mm).
8. Regular medication, which may interfere with antimalarial pharmacokinetic
9. History of hypersensitivity reactions or contraindications to any of the medicine(s) being tested or used as alternative treatment(s)

Date of first enrolment

15/09/2015

Date of final enrolment

30/03/2017

Locations**Countries of recruitment**

Uganda

Study participating centre**Arua Hospital**

Arua District

East Africa Public Health Laboratory Network (EAPHLN) site

Uganda

-

Study participating centre**Mbarara Hospital**

Mbarara District

East Africa Public Health Laboratory Network (EAPHLN) site

Uganda

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Study participating centre**Nagongera Health Centre IV**

Tororo District

Uganda Malaria Surveillance Project (UMSP) sentinel site

Uganda

-

Sponsor information

Organisation

Uganda Ministry of Health

Sponsor details

East Africa Public Health Laboratory Networking Project

Kampala

Uganda

-

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Sponsor type

Government

ROR

<https://ror.org/00hy3gq97>

Funder(s)

Funder type

Government

Funder Name

The World Bank

Funder Name

Ministry of Health, Uganda

Results and Publications

Publication and dissemination plan

Study results shall be disseminated to health authorities in Uganda and the East African region. The findings from this study shall be published in peer reviewed journals. Results shall further be presented at scientific meetings and conferences.

Intention to publish date

01/12/2017

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

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/03/2019	14/01/2020	Yes	No