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

Submission date
17/08/2015

Recruitment status
No longer recruiting

Registration date
20/10/2015

Overall study status
Completed

Last Edited
14/01/2020

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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-piperaquine (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 Hosptial (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
yadoke@yahoo.com

Contact information

Type(s)
Scientific

Contact name
Dr Adoke Yeka

Contact details
Makerere University School of Public Health
College of Health Sciences
Kampala
Uganda
-
+256 772 473533
yadoke@yahoo.com

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 Pneumocisti carini 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
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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
-
+256 414 231584
deuslukoye@yahoo.com

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 Ugaanda 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