ISRCTN78910521 https://doi.org/10.1186/ISRCTN78910521

Study of the artemether-lumefantrine combination for the treatment of uncomplicated Malaria in Bengo Province, Angola

Submission date
13/12/2022

Recruitment status
No longer recruiting

Registration date
26/04/2023

Overall study status
Completed

Last Edited
26/04/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Artemether-Lumefantrine (AL) is the most used antimalarial worldwide, and the most frequently adopted first-line antimalarial drug by National Malaria Control Programs. However, slowly but progressively, Plasmodium falciparum (malaria) has been developing ways to evade AL action. In Angola, AL efficacy trials reported efficacies below the WHO threshold for acceptable artemisinin-based combination therapy (ACT) cure rates (90 %) for the provinces of Zaire and Lunda Sul. Thus, close monitoring of AL efficacy is essential.

Who can participate?
Children aged 2 to 10 years old, with malaria infection.

What does the study involve?
A blood sample (venous harvesting) was required before treatment initiation. AL therapy was immediately initiated, with the patients being hospitalized for the full duration of the treatment course, under 24-hour vigilance by a qualified nurse, with regular (daily) visits from the medical doctors. During this inpatient period, blood sampling (digital, filter paper preserved) was performed at 24 and 48 hours and a minimum of 12 hours after the last dose. Before leaving the premises, the patient was monitored for his/her general clinical condition, haemoglobin levels and parasitemia and/or fever, in accordance with the WHO criteria for the definition of early treatment failure (ETF). The trial also included a 42-day follow-up in order to detect late recrudescences, as frequently observed in previous clinical trials, namely with AL. The active (search and transport of patient) follow-up included weekly clinical/parasitological check-ups at the health center, starting on day 7, and then on days 14, 21, 28, 35 and 42.

What are the possible benefits and risks of participating?
Procedures, drugs and all other consumables will be provided entirely for free. Besides the inpatient maintenance (food, specific care), the patients had access to entertainment activities, in conformity with the targeted age group. The risk of participation is smaller than that involved

with a routine non-supervised uncomplicated treatment in accordance with the national health guidelines.

Where is the study run from?
The study was performed at Centro de Saúde Materno-Infantil das Mabubas, Dande Municipality, Bengo Province ((population: ca. 360,000, with 41% of the population < 15-year-old)), involving fever cases admitted from the urgency board. The Mabubas community is approximately 70 Km northeast of Luanda.

When is the study starting and how long is the expected to run for?
October 2018 to December 2021

Who is funding the study?
1. Fundação para a Ciência e Tecnologia, Ministério da Ciência e Ensino Superior, Portugal
2. Aga Khan Development Network (AKDN)
3. Calouste Gulbenkian Foundation (Portugal)

Who is the main contact?
Pedro Gil, jose.pedro.gil@ki.se

Study website
http://www.cisacaxito.org/pt/areas/research/malango/

Contact information

Type(s)
Scientific

Contact name
Prof José Gil

ORCID ID
http://orcid.org/0000-0002-6107-9379

Contact details
Department of Microbiology, Tumor and Cell Biology (MTC)
Karolinska Institutet (Biomedicum)
Solnavägen 9, C9
Solna
Sweden
17165
+46 70 9358556
jose.pedro.gil@ki.se

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Efficacy trial on direct observed artemether-lumefantrine treatment

Acronym
MalAngo

Study objectives
The corrected cure rates of artemether-lumefantrine in the Bengo province of Angola are significantly above the 90% World Health Organization (WHO) threshold for an acceptable ACT performance.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/10/2018, Ethics Committee of the Ministry of Health of the Republic of Angola (Instituto Nacional de Investigação em Saúde, Rua Amílcar Cabral 96, Maianga - Luanda Angola; +244222393247; geral@inis.ao, inis.minsa@gmail.com), ref: 292018

Study design
Open-label phase 4 randomized one-arm 3-day artemether-lumefantrine (six doses) trial

Primary study design
Interventional

Secondary study design
Randomised controlled 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
Treatment of non-complicated malaria in children aged 2 to 10 years old

Interventions

This is a single-arm trial, in which a sample of children with non-complicated malaria is given artemether-lumefantrine (6 doses/3 days) and followed over time to observe their response to the drug. Therefore, no control group is included, and no randomization is performed. A weekly recruitment procedure is performed until reaching the enrolment of up to 3 patients. Participants will receive six doses of artemether-lumefantrine (artemether 20 mg + lumefantrine 120 mg), as required. The time points of blood sampling will be as such: 0, 8, 24, 36, 48, and 60 hours. During this period, the patients will be under 24-hour vigilance by a qualified nurse, with regular (daily) visits from medical doctors. The patients will be hospitalized until a minimum of 12 hours after the last dose. This implies that the patient will only leave the ward by the first post-treatment conclusion day (day 3). Before leaving the premises, the patient will be monitored for haemoglobin levels and parasitemia and/or fever, in accordance with the WHO definition of early treatment failure (ETF). The trial also includes a long 42-day follow-up in order to detect late recrudescences, as frequently observed in previous clinical trials, namely with artemether-lumefantrine. The follow-up will include weekly clinical check-ups at the hospital, starting on day 7, and then on days 14, 21, 28, 35 and 42.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Artemether, lumefantrine

Primary outcome measure
The number of PCR-corrected recrudescent infections among 2–10-year-old patients with P. falciparum non-complicated malaria by day 28 post-treatment initiation

Secondary outcome measures
1. The PCR-corrected efficacy (per protocol) values by day 42
2. PCR corrected reinfection rates by day 42

Overall study start date
02/10/2018

Completion date
13/12/2021

Eligibility

Key inclusion criteria
1. Children ≥2, ≤10-year-old, both sexes.
2. Body weight. We assume the upper 50% quartile (WHO child growth reference, WHO http://www.who.int/childgrowth/standards/weight_for_age/en/) for inclusion, i.e. ≥9 Kg, with no evidence of severe sub-nutrition.
3. Plasmodium falciparum non-complicated malaria defined by axillar temperature ≥37.5°C (oral /rectal/tympanum ≥38°C) + microscopically confirmed Plasmodium falciparum parasitemia >1, 000 ≤200,000 parasites/µL.
4. Written informed consent by the Patient’s Guardian.

5. Capacity to swallow medication.
6. Absence of antimalarial exposure during the last two weeks.
7. Having residence inside the CISA Demographic Survey Project

Participant type(s)
Patient

Age group
Child

Lower age limit
2 Years

Upper age limit
10 Years

Sex
Both

Target number of participants
100

Total final enrolment
100

Key exclusion criteria
1. Symptoms of severe malaria, requesting specific parental treatment, in accordance with WHO guidelines.
2. Oral treatment intolerance, including gastro-intestinal events (e.g. repeated vomiting or severe diarrhea) incompatible with an adequate drug absorption.
3. Clinical History or recent events of potentially confounding acute or chronicle conditions.
4. Anaemia at arrival (Hb <7g/dL)
5. Fever caused by conditions other than malaria.
6. Documented hyper-sensitivity to lumefantrine and artemisinin compounds.
7. Treatment with antimalarial in the last two weeks.

Date of first enrolment
01/12/2020

Date of final enrolment
01/11/2021

Locations

Countries of recruitment
Angola

Study participating centre

Health Research Center of Angola (CISA)
Rua direita de Caxito
Hospital Geral do Bengo
Bengo
Angola
-

Sponsor information

Organisation
Hospital Pediátrico David Bernardino - Dr. Luís Bernardino

Sponsor details
Rua Amilcar Cabral
Luanda
Angola
-
+244 928133812
nid@hpdb.gov.ao

Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
Fundação para a Ciência e a Tecnologia (FCT)

Funder Name
Aga Khan Foundation

Alternative Name(s)
AKF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Funder Name
Calouste Gulbenkian Foundation (FCG)

Results and Publications

Publication and dissemination plan
Scientific international peer reviewed publications, international meetings, social media outlets, audio-visual tools.

Intention to publish date
15/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. José Pedro Gil (jose.pedro.gil@ki.se)

IPD sharing plan summary
Available on request