

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	<input type="checkbox"/> Prospectively registered
Registration date 26/04/2023	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 26/04/2023	Condition category Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Protocol serial number

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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 $\geq 37.5^{\circ}\text{C}$ (oral /rectal/tympanum $\geq 38^{\circ}\text{C}$) + microscopically confirmed *Plasmodium falciparum* parasitemia $> 1,000 \leq 200,000$ 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

Healthy volunteers allowed

No

Age group

Child

Lower age limit

2 years

Upper age limit

10 years

Sex

All

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
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Sponsor information**Organisation**

Hospital Pediátrico David Bernardino - Dr. Luís Bernardino

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes