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Adherence to malaria treatment policy and prevalence of Pfkelch13 and background mutations associated with artemisinin resistance emergence in Plasmodium falciparum parasites in Uganda

Submission date	Recruitment status	[_] Prospectively registered
25/03/2022	No longer recruiting	[_] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
01/04/2022	Completed	[_] Results
Last Edited	Condition category	[_] Individual participant data
28/03/2022	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Malaria is a serious and sometimes fatal disease caused by a parasite that commonly infects a certain type of mosquito which feeds on humans.
Malaria remains a serious public health problem in Uganda, accounting for 30-50% of out-patient visits, 15-20% of hospital admissions and up to 20% of in-patient deaths. Malaria treatment is threatened by resistance to artemisinin agents, the cornerstone of current treatment modalities. Artemisinins are derived from extracts of sweet wormwood (Artemisia annua) and are well established for the treatment of malaria, including highly drug-resistant strains.
Efforts to track and contain artemisinin resistance especially in sub-Saharan Africa are hindered by lack of valid molecular markers coupled with inadequate capacity to perform routine parasite sensitivity analysis. Additionally, lack of information on local drivers of artemisinin resistance development and spread further limit development of containment and eradication strategies.
The study is screening for the presence of artemisinin resistance in Plasmodium falciparum parasites among symptomatic malaria patients in low and high malaria transmission settings in Uganda

Who can participate?
Adult (18 years and above) malaria patients

What does the study involve?
Participants provide a blood sample at a single time point

What are the possible benefits and risks of participating?
There are no anticipated direct benefits and risks to participating in this study. However, participating in the study will help in advancing scientific knowledge on artemisinin resistance.

Where is the study run from?
Makerere University, College of Health Sciences, Department of Pharmacology & Therapeutics (Uganda)

When is the study starting and how long is it expected to run for?
August 2019 to December 2023

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

Who is the main contact?
Dr Moses Ocan, ocanmoses@gmail.com

Contact information

Type(s)
Principal Investigator

Contact name
Dr Moses Ocan

ORCID ID
http://orcid.org/0000-0002-8852-820X

Contact details
Upper Mulago Hill Road
Kampala
Uganda
-
+256 782355302
moses.ocan@mak.ac.ug

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SBS 803

Study information

Scientific Title
Predictors of local emergence and spread of artemisinin resistance among Ugandan plasmodium falciparum parasites

Acronym
Pfkelch13 emergence

Study objectives
Research questions
1. What is the extent of adherence to national malaria treatment guidelines/policy in malaria treatment in private hospitals, private pharmacies and public hospitals in low and high malaria transmission settings in Uganda
2. What is the prevalence of Pfkelch13 single nucleotide polymorphisms and background mutations fd (ferredoxin), arps10 (apicomplast ribosomal protein S10), mdr-2 (multi-drug resistance protein-2) and crt (chloroquine resistance protein) in Plasmodium falciparum parasites in low and high malaria transmission settings in Uganda

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/10/2020, School of Biomedical Science Research Ethics Committee (P.O. Box 7072, Kampala, Uganda; +256 752575050; biomedicalresearch62@gmail.com), ref: SBS 803

Study design
Single center observational cross-sectional cohort study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not applicable

Health condition(s) or problem(s) studied
Screening for occurrence of artemisinin resistance among symptomatic malaria patients

Interventions
The study is screening for the presence of artemisinin resistance in Plasmodium falciparum parasites among symptomatic malaria patients in low and high malaria transmission settings in Uganda. Microscopy is being used to screen for the presence of Plasmodium falciparum parasites in blood samples collected from malaria symptomatic patients. For blood samples where malaria parasites are confirmed, the sample is collected in a dried blood spot Whatman filter paper. The DNA of the parasites are then extracted from the filter paper and screened for the presence of K13 mutations (markers for artemisinin resistance) and background mutations (crt, arps10, fd, mdr-2) using Sanger sequencing method

Approach: (i) Treatment of malaria patients in health facilities (public and private) will be assessed using a checklist to establish adherence to national malaria treatment guidelines, (ii) P. falciparum infected blood samples collected in high and low malaria transmission settings in Uganda will be used. P. falciparum infection will be established using PfHRP-2 Rapid Diagnostic Test (HRP-2 RDT) and microscopy. (iii) Parasite DNA will be extracted and purified using Qiagen-Max kit. Next generation sequencing platform will be used to establish Pfkelch13 Single nucleotide polymorphisms (SNPs) and genetic background mutations (fd, arps10, mdr2 and crt) in P. falciparum parasites.

Intervention Type
Other

Primary outcome measure
Artemisinin resistance is measured using K13 gene mutations and background mutations (crt, arps10, fd, mdr-2) at baseline. This being a cross-sectional study, the outcome will be measured once at baseline.

Secondary outcome measures
1. Level of adherence to malaria treatment policy measured using a questionnaire and interview guide at baseline
2. Pharmacopoeial quality of ACTs measured using LC-MS at baseline

Overall study start date
10/08/2019

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Symptomatic malaria patients
2. Age 18 years and above
3. Patients with malaria treatment given at a hospital

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

Total number of patients 385 (Tororo general hospital, 150; Apac general hospital, 150; Mbarara regional referral hospital, 45; Kabale regional referral hospital, 40)

Key exclusion criteria
1. Severely ill adult malaria patients
2. Anemic patients (males, Hb < 13g/100ml; non-pregnant females, Hb <12g/100ml; pregnant females, Hb <11g/100ml)
3. Patients with low parasite load (<1000 parasites/µl of blood)

Date of first enrolment
05/06/2021

Date of final enrolment
05/06/2022

Locations

Countries of recruitment
Uganda

Study participating centre
Makerere University
College of Health Sciences
Department of Pharmacology & Therapeutics
Upper Mulago Hill Road
Kampala
Uganda
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Sponsor information

Organisation
European & Developing Countries Clinical Trials Partnership

Sponsor details
PO Box 93015
The Hague
Netherlands
2509 AA
+31 70 344 0880
edctpgrants@edctp.org

Sponsor type
Research organisation

Website
http://www.edctp.org/

ROR
https://ror.org/031jv9v19

Funder(s)

Funder type
Government

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
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, The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Publication and dissemination plan
The research outputs will be communicated to, Ministry of Health (Malaria Control Program), Scientific community, Community engagement. In community engagement, different stakeholders such as Non-governmental organizations (MeTA, HEPS-Uganda), healthcare professionals through professional organizations (Uganda Medical Association, Uganda Pharmaceutical Society, Uganda Pharmacological Society, Uganda Nurses and Midwives Union), patients/local communities. This will be done through workshops with the stakeholders. For patient/local communities, one member of a Village Health Team (VHT) from each of the study districts will be invited for the stakeholder dialogue and results dissemination. The invited VHTs will then organize local workshops with other VHTs in the study districts. The VHTs will then share key study findings with local communities during their routine service to communities.

In addition, the project website will provide a platform for the public to know about the study. The website will be developed at project month 1.

Stakeholder meetings: The research outputs will be shared with the stakeholders (Ministry of Health, Scientific community/researchers, Non-governmental organizations, and healthcare professionals) through meetings. The meeting will involve oral presentation of project research outputs and dialogue with the audience. This will be done once every 6 months throughout the project duration.
Report writing: The key research findings will summarized in a book (research report). The report will then be distributed to the libraries of Ministry of Health and Universities that train Medical Students in Uganda. The report will also be shared with the Non-governmental organizations and health professional organizations.
Publications: Three articles from the findings of the project will be published in open access peer reviewed journal.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
Primary data will be shared with open access journals where the study will be published.

IPD sharing plan summary
Published as a supplement to the results publication