

Primaquine in African Children: PAC study

Submission date 17/03/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 09/05/2017	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 20/10/2025	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Malaria is a disease that is spread by mosquito bites. It causes flu-like symptoms but can also cause serious illness and death. Malaria is a major problem in tropical areas like Africa. Research has shown that a drug called primaquine can reduce the malaria offspring in mosquitos which can then reduce malaria transmission. However, primaquine has a major disadvantage as it changes to act like bleach in the body. This is problematic to people who have naturally weak red blood cells and are lacking an enzyme that makes the chemicals that counteract bleach and drug metabolites called glucose 6 phosphate dehydrogenase (G6PD). The less G6PD in the red cells, the more damaging primaquine's is. It can cause red cells may burst open (haemolysis) which creates many health problems. Many malaria control programmes are unwilling to use primaquine because they think it is too dangerous and they cannot afford the cost, training or equipment to test for G6PD levels. Although the World Health Organisation (WHO) recommends using low dose primaquine even in malaria patients with G6PD deficiency, primaquine is not being used due to a lack of research, concerns about tests for G6PD and issues providing the medication to children. The aim of this study is to provide evidence that a low dose of primaquine is safe in G6PD deficient kids in order to reduce malaria rates and benefit communities.

Who can participate?

Children aged six months to 11 years old who have malaria.

What does the study involve?

Participants are allocated to one of two groups. Those in the first group have a deficiency in G6PD and those in the second group have normal G6PD levels. Participants in each group are then randomly allocated to one of four dosing treatments which include primaquine and combination treatments and two placebo primaquine treatment. The doses vary with each participant's age and weight and are given daily for three days. The placebo group only receives the medication once. Participants are followed up for 42 days to measure their iron deficiency level in their blood.

What are the possible benefits and risks of participating?

Participants may benefit from knowing the status of their G6PD levels and from receiving information and counseling. There are risks with primaquine as it can cause anaemia (low blood iron).

Where is the study run from?

1. Kinshasa Mahidol Oxford Tropical Medicine Research Unit (Democratic Republic of Congo)
2. The Mbale Regional Referral Hospital (Uganda)

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

February 2017 to November 2020

Who is funding the study?

DFID/MRC/Wellcome Trust (UK), grant reference number: MR/P006973/1

Who is the main contact?

Dr Bob Taylor

Contact information

Type(s)

Public

Contact name

Dr Bob Taylor

Contact details

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Additional identifiers

Protocol serial number

BAKMAL1606, 106698/Z/14/Z

Study information

Scientific Title

Assessing the tolerability and safety of single low dose primaquine in African children with acute uncomplicated falciparum malaria and glucose 6 phosphate dehydrogenase deficiency in Africa

Acronym

PAC study

Study objectives

The aim of this study is to provide evidence for drug policy on the safety of the WHO recommended SLDPQ regimen when used under close to routine conditions to G6PDd African children with acute uncomplicated P. falciparum.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Oxford Tropical Research Ethics Committee, 01/03/2017, ref: 53-16

Study design

Multi-centre double-blind open randomized parallel safety trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Uncomplicated falciparum Malaria, G6PD deficiency, Single low dose primaquine (SLDPQ)

Interventions

Participants are allocated to either the G6PDd group or the G6PD normal group based on their the results of a G6PD rapid diagnostic test (RDT).

Participants are then randomly allocated as to which dosing group they receive using a computer generated randomisation list generated for each site. Treatment allocation is placed in a sealed envelope which is opened once participants receive their study number. The treatment allocation described the Artemisinin based combination treatment (ACT) to be given and the number of PQ/placebo pack.

The four dosing groups are the following:

1. Artemether Lumefantrine (AL) + single low-dose primaquine (SLDPQ)
2. Artemether Lumefantrine (AL) + single low-dose primaquine (SLDPQ) placebo
3. Dihydroartemisinin-piperaquine (DHAPP) + single low-dose primaquine (SLDPQ)
4. Dihydroartemisinin-piperaquine (DHAPP) + single low-dose primaquine (SLDPQ) placebo

The dosages for primaquine depends vary with age and the dosing for AL vary with weight (in kg). DHAPP+SLDPQ dosages are given daily for three days and vary with body weight (in kg). Those who receive the primaquine/placebo receive it once only at baseline. Follow up continues until day 42.

Intervention Type

Drug

Phase

Phase III/IV

Drug/device/biological/vaccine name(s)

Artemether, lumefantrine, dihydroartemisinin, piperaquine, primaquine

Primary outcome(s)

1. Profound anaemia (Hb concentration < 4g/dL) is measured using the HemoCue machine during the first days 21 days of follow up

2. Severe anaemia (Hb <5g/dL) with clinical features of severe malaria is measured using the HemoCue machine during the first 21 days of follow up

Key secondary outcome(s)

1. Fractional change in haemoglobin on day seven vs. baseline, measured by HemoCue® at baseline and day seven
2. Proportion of patients with a fractional change of $\geq 25\%$ measured by HemoCue® over the follow up period of 42 days
3. Determinants of changes in HemoCue® measured haemoglobin over the follow up period of 42 days
4. G6PD genotype (hemizygous male, homo-, heterozygous female, normal) and selected G6PD variants (e.g. G6PD A- 202 mutations) are assessed by polymerase chain reaction (PCR) at baseline
5. G6PD enzyme activity is measured using a quantitative spectrophotometric method at baseline
6. Genotypes of other inherited blood disorders are assessed by polymerase chain reaction (PCR) at baseline
7. Incidence of adverse events are measured using clinical and laboratory records over the follow up period of 42 days
8. Pharmacokinetic characteristics of PQ and carboxyPQ by measuring drug concentrations at baseline and at hours one, one and a half, two, three, four, six, eight, ten, 12, 24 hours
9. Pharmacokinetic characteristics of lumefantrine and piperaquine are measured using their drug concentrations at baseline, day three, seven and 28
10. CYP 2D6 genotypes are assessed by polymerase chain reaction (PCR) at baseline
11. Asexual parasitaemia clearance time and half life are measured using malaria slide results at days one, two and three
12. Therapeutic efficacy of AL and DHAPP is measured using the WHO criteria at day 42
13. Gametocytaemia over time is measured using thick blood films at baseline and days one, two, three, seven, 14, 21, 28, 35 and 42
14. Proportion of patients with gametocytes over time is measured using those with a positive thick blood film at baseline and on days one, two, three, seven, 14, 21, 28, 35 and 42

Completion date

02/11/2020

Eligibility

Key inclusion criteria

1. Aged 6 months to 11 years old
2. Clinically uncomplicated disease
3. Fever ($\geq 37.5^{\circ}\text{C}$ aural) or history of fever within the previous 72 hours
4. Positive malaria RDT (Uganda only)
5. Positive malaria slide for *P. falciparum* (mono or mixed infection) of any parasitaemia (Kinshasa only)
6. Informed consent provided by patient or relative/legal guardian

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Lower age limit

6 months

Upper age limit

11 years

Sex

All

Total final enrolment

1137

Key exclusion criteria

1. Malaria danger signs, sign(s) of severe malaria, or decompensated anaemia, including: an inability to take or retain fluids or oral medications, confusion, prostration, convulsions, respiratory distress, passing of red or cola-coloured urine (putative "blackwater fever")
2. Severe anaemia (Hb <6 g/dL)
3. Comorbid illness that requires treatment in hospital (physician's judgement)
4. Patients on drugs known to cause haemolysis in G6PDd e.g. dapsone, nalidixic acid
5. Known to be allergic to PQ, AL, or DHAPP
6. Previous enrolment in the current trial or current enrolment in another trial

Date of first enrolment

17/07/2017

Date of final enrolment

07/10/2019

Locations**Countries of recruitment**

Congo, Democratic Republic

Uganda

Study participating centre

Kinshasa Mahidol Oxford Tropical Medicine Research Unit

The Kinshasa School of Public Health

University of Kinshasa

Avenue Tombalbaye 68-78

Kinshasa

Congo, Democratic Republic

1015

Study participating centre
The Mbale Regional Referral Hospital
Mbale Clinical Research Institute
Mbale Regional Referral & Teaching Hospital
Mbale
Uganda
209

Sponsor information

Organisation
The University of Oxford

ROR
<https://ror.org/052gg0110>

Funder(s)

Funder type
Other

Funder Name
DFID/MRC/Wellcome Trust

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary

Available on request

Study outputs

Output type Details

[Results article](#)

[Results article](#)

[Results article](#)

Date created	Date added	Peer reviewed?	Patient-facing?
30/11/2022	05/12/2022	Yes	No
20/10/2023	20/10/2023	Yes	No
01/07/2025	02/07/2025	Yes	No

Results article	Plasma folate dynamics in Plasmodium falciparum-infected African children treated with artemisinin combination therapy and single low-dose primaquine or placebo	15/10/2025	20/10/2025	Yes	No
Other publications	Age-based dosing regimen development	18/01/2018	21/10/2021	Yes	No
Other publications	Pharmacokinetics	25/09/2023	09/06/2025	Yes	No
Participant information sheet	version V2	14/02/2017	01/06/2017	No	Yes
Participant information sheet	version V2	14/02/2017	01/06/2017	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2	01/09/2018	22/08/2022	No	No