

A randomised, controlled, open-label, parallel-group study comparing the efficacy and safety of an oral artesunate-amodiaquine fixed-dose combination therapy over 3 subsequent days to an equivalent dose regimen of the individual drugs for the treatment of children with *Plasmodium falciparum*

Submission date 26/11/2007	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 29/11/2007	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 28/03/2017	Condition category Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

RPC082

Study information

Scientific Title

A randomised, controlled, open-label, parallel-group study comparing the efficacy and safety of an oral artesunate-amodiaquine fixed-dose combination therapy over 3 subsequent days to an equivalent dose regimen of the individual drugs for the treatment of children with Plasmodium falciparum

Study objectives

This trial consists of two studies: the efficacy/safety study and the efficacy/safety/Pharmacokinetic (PK) study

Primary objective (for both efficacy/safety and efficacy/safety/PK studies): To show the non-inferiority in terms of efficacy of the fixed combination AmodiaQuine (AQ)/ArteSunate (AS) compared to both drugs taken separately

Secondary objectives:

1. To evaluate treatment tolerability and safety in all participants (890 patients)
2. To evaluate the PK of AS and AQ in 140 patients

Ethics approval required

Old ethics approval format

Ethics approval(s)

The World Health Organization (WHO)/Scientific Committee for Research In Human Subjects (SCRIHS), 19/10/2004

Study design

Open-label parallel-group multi-centre (two centres) randomised controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied

Malaria

Interventions

The overall trial start and end dates above refer to the efficacy/safety study. The overall trial start and end dates of the study with PK are September 2006 and December 2006, respectively.

Patients will be equally randomized into the following treatment groups:

1. Fixed dose AS/AQ combination - Tablets containing 25 mg AS and 67.5 mg AQ, 1 tablet per day for children aged 0-11 months; 2 tablets per day for children aged 1-5.
2. AS (50 mg) + AQ (153 mg). 1/2 AS tablet and 1/2 AQ tablet per day for children aged 0-11 months; 1 AS tablet and 1 AQ tablet per day for children aged 1-5 years.

Duration of treatment: 3 consecutive days

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Artesunate, amodiaquine

Primary outcome measure

To show the non-inferiority in terms of efficacy of the fixed-dose combination AQ/AS compared to both drugs given separately. Efficacy will be measured by:

1. Cure rate (elimination of parasitemia without relapse) 28 days after the beginning of treatment
2. Parasitemia reduction rate and parasite clearance time (Duration of follow-up: 28 days)
3. Fever clearance time (Duration of follow-up: 28 days)
4. Gametocyte carrier rate (Duration of follow-up: 28 days)

Secondary outcome measures

Tolerance and safety. The following will be evaluated at each visit until day 28 (Day 0, 1, 2, 3, 7, 14, 21 and 28):

1. Clinical tolerance and safety, measured by the following:
 - 1.1. Signs/symptoms which may appear after the treatment
 - 1.2. Serious adverse events
 - 1.3. In study with PK only: ElectroCardioGram (ECG) anomalies (prolonged QT interval).Measured at day 0, 2 and 28

2. Biological tolerance and safety. The following will be measured by blood tests at day 0, 7 and 28 (If abnormal values are found at day 7 or day 14, the measurements will also be carried out on day 14 and 21 in addition to day 28):

- 2.1. Biochemical tests:
 - a. Alanine AminoTransferase [ALAT]

b. Bilirubin

c. Creatinine

2.2. Hematological tests:

a. Complete Blood Count [CBC]

3. In study with PK only: PK parameters (Population PK, AUC, Cmax, Tmax, T1/2)

Overall study start date

01/10/2004

Completion date

28/02/2006

Eligibility

Key inclusion criteria

1. Patient between 6 months and <5 years old
2. Bodyweight \geq 5 kg (to help the assay of artesunate)
3. *P. falciparum* single-species infection with positive parasitemia (asexual forms) greater than 1,000 parasites per microlitre of blood
4. Fever (uncorrected axillary temperature $>37.5^{\circ}\text{C}$) on Day 0 in children
5. No other obvious cause for the fever (e.g., respiratory [ear, nose and/or throat] infection)
6. Consent of the child's family or guardian

Participant type(s)

Patient

Age group

Child

Lower age limit

6 Months

Upper age limit

5 Years

Sex

Both

Target number of participants

750 for efficacy/safety study; 140 for study with PK (total: 890 participants)

Key exclusion criteria

1. Signs of life threatening and/or severe malaria
2. Other underlying diseases (cardiac, renal, hepatic, severe malnutrition)
3. Allergy to the study drugs
4. Treatment with amodiaquine within the past 7 days, or with artemisinin derivatives within the past 3 days (72 h)

5. Complete cure with an antimalarial within the past 7 days (with the exception of chloroquine)
6. On-going treatment with an antibiotic with antimalarial action (e.g. co-trimoxazole, tetracycline, or macrolide)

Date of first enrolment

01/10/2004

Date of final enrolment

28/02/2006

Locations

Countries of recruitment

Burkina Faso

Study participating centre

Centre National de Recherche et de Formation sur le Paludisme (CNRFP)

Ouagadougou

Burkina Faso

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Sponsor information

Organisation

Drugs for Neglected Diseases initiative (DNDi) (Switzerland)

Sponsor details

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Sponsor type

Research organisation

Website

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ROR

<https://ror.org/022mz6y25>

Funder(s)

Funder type

Research organisation

Funder Name

Drugs for Neglected Diseases initiative (DNDi) (Switzerland)

Funder Name

Ministerie van Buitenlandse Zaken

Alternative Name(s)

Dutch Ministry of Foreign Affairs, Ministry of Foreign Affairs, Ministry of Foreign Affairs of the Kingdom of the Netherlands

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Netherlands

Funder Name

Medecins Sans Frontieres (MSF) (International)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details results	Date created	Date added	Peer reviewed?	Patient-facing?
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Results article		16/03/2009	Yes	No
Results article	results	20/08/2009	Yes	No