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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

Registration date
29/11/2007

Overall study status
Completed

Last Edited
28/03/2017

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 >= 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°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
15 Chemin Louis Dunant
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CH-1202
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Sponsor type
Research organisation

Website
http://www.dndi.org/

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	Date created	Date added	Peer reviewed?	Patient-facing?
	results				

Results article	results	16/03/2009	Yes	No
Results article		20/08/2009	Yes	No