ISRCTN70618692 https://doi.org/10.1186/ISRCTN70618692

Assessment of efficacy, safety and population-pharmacokinetics of the fixed-dose combination of artesunate-mefloquine in the treatment of acute uncomplicated Plasmodium falciparum malaria in India

Submission date 21/11/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/11/2008	**Overall study status** Completed	
Last Edited 28/03/2017	**Condition category** Infections and Infestations	

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

DND-ASM-07

Study information

Scientific Title
Assessment of efficacy, safety and population-pharmacokinetics of the fixed-dose combination of artesunate-mefloquine in the treatment of acute uncomplicated Plasmodium falciparum malaria in India

Study objectives
1. To evaluate the clinical and parasitological efficacy of artesunate-mefloquine fixed-dose combination in adult patients with uncomplicated falciparum malaria, by determining the proportion of patients achieving a negative parasitaemia without recrudescence by 63 days (cure rate)
2. To measure the parasite reduction ratio at 48 hours of treatment, parasite clearance time, fever clearance time, gametocyte carriage
3. To evaluate cure rate at 28 days
4. To evaluate the population-pharmacokinetics of artesunate-mefloquine in adult patients in India
5. To evaluate the incidence of adverse events
6. To collect information to enable the Ministry of Health to make informed decisions about the possible need for updating of the current national anti-malarial treatment guidelines

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Ethics Committee of the National Institute of Malaria Research (ICMR), 23/10/2007

Study design
Multicentre single-arm open-label clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
All patients recruited into the study will be given full, supervised treatment with oral artesunate-mefloquine 100 mg and 220 mg tablets (two tablets daily for three days). Total duration of treatment and follow-up is 3 days of treatment and 60 days of follow-up.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Artesunate, mefloquine

Primary outcome measure
Cure rate as determined by polymerase chain reaction (PCR)-corrected adequate clinical and parasitological response (ACPR) on day 63. Treatment success or failures will be classified according to WHO Guidelines 2005.

Secondary outcome measures
1. Pharmacokinetic parameters: population pharmacokinetic parameters for artesunate (AS), dihidroartemisinin (DHA), and mefloquine (MQ)
2. Parasite reduction ratio (PRR) at 48 hours: baseline parasite count/parasite count at 48 hours
3. Parasite clearance time (PCT): time in hours from the initiation of therapy until the first of two successive (within an interval of 8 to 24 hours) parasite negative smears are obtained
4. Fever clearance time (FCT): time in hours from the initiation of therapy until disappearance of fever for at least 24 hours
5. Gametocyte carriage: percentage of patients without gametocytes at day 28
6. Proportion of patients with early treatment failure, late treatment failure, and late parasitological failure
7. Proportion of patients with mixed infections in the follow-up assessments
8. Proportion of patients with development of symptoms of severe malaria

Overall study start date
01/12/2007

Completion date
31/12/2008

Eligibility

Key inclusion criteria
1. Male or female patients greater than or equal to 18 years of age
2. Presence of acute uncomplicated P. falciparum mono-infection confirmed by:
2.1. Fever, as defined by axillary temperature greater than or equal to 37.5°C or history of fever in the previous 24 hours, and
2.2. Positive microscopy of P. falciparum with parasite density between 1,000 and 100,000 asexual parasite count/µl of blood
3. Written informed consent provided by patient; if the patient is unable to write, witnessed consent is permitted according to local ethical considerations

4. Screening laboratory values within the following limits:
4.1. Haemoglobin (Hb) greater than or equal to 7 g/dl
4.2. Total bilirubin less than or equal to 2.5 times upper limit of normal (ULN)
4.3. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) less than or equal to 2.5 times ULN
4.4. Serum creatinine less than or equal to 1.5 times ULN
5. Negative urine pregnancy test before the first dose of fixed-dose combination (FDC) if the subject is a female of childbearing potential

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
84 patients

Key exclusion criteria
1. Patients with signs and symptoms of severe/complicated malaria requiring parenteral treatment according to the World Health Organization Criteria 2000 (Annex 1)
2. Mixed Plasmodium infection
3. Known history or evidence of clinically significant disorders such as cardiovascular (including arrhythmia), respiratory (including active tuberculosis), hepatic, renal, gastrointestinal, immunological (including active human immunodeficiency virus [HIV]/acquired immune deficiency syndrome [AIDS]), neurological (including auditory), endocrine, infectious, malignancy, psychiatric (active depression, recent history of depression, generalised anxiety, psychosis, schizophrenia or other major psychiatric disorders), history of convulsions or other abnormality (including recent head trauma)
4. Presence of febrile conditions caused by diseases other than malaria
5. Known history of hypersensitivity, allergic or serious adverse reactions to mefloquine, quinine, quinidine, artesunate or other artemisinins
6. History of use of any other anti-malarial agent within 2 weeks prior to start of the study
7. Except for women of non-childbearing potential sexually active individuals participating in the study must agree to use a medically acceptable form of contraception during the study and for at least 15 days after day 63
8. Received an investigational drug within the past 4 weeks
9. Inability to swallow oral medication

Date of first enrolment
01/12/2007

Date of final enrolment
31/12/2008

Locations

Countries of recruitment
India

Study participating centre
National Institute of Malaria Research
New Delhi
India
110029

Sponsor information

Organisation
Drugs for Neglected Diseases initiative (DNDi) (Switzerland)

Sponsor details
15 Chemin Louis Dunant
Geneva
Switzerland
CH-1202

Sponsor type
Research organisation

Website
http://www.dndi.org/

ROR
https://ror.org/022mz6y25

Funder(s)

Funder type
Government

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
Spanish Agency for International Cooperation (Agencia Espanola de Cooperacion Internacional) (Spain)

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 article	results	23/05/2014		Yes	No
Results article	results	28/12/2015		Yes	No