

Study of resistance to artesunate of malaria parasite

Submission date 22/01/2008	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 25/01/2008	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 21/03/2013	Condition category Infections and Infestations	<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
Version 12 Dec 2007

Study information

Scientific Title

Clinical investigation of in-vivo and in vitro susceptibility of *P. falciparum* to artesunate in Western Thailand

Study objectives

Has the resistance to artemisinins in *P. falciparum* emerged in Thailand?

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from Mahidol University Ethical Committee on the 20th December 2007 (ref: MUTM 2007-130).

Study design

Pharmacokinetic and dynamic study of artesunate in two randomly assigned treatment groups.

Primary study design

Interventional

Secondary study design

Non randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

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

Health condition(s) or problem(s) studied

Malaria/uncomplicated/resistance

Interventions

Patients will be randomised in blocks of 10 to receive either:

1. Artesunate (Guilin Pharmaceutical Company, PRC) orally (po) 2 mg/kg/day for 7 days
2. Artesunate (Guilin Pharmaceutical Company, PRC) po 4 mg/kg/day for 3 days plus mefloquine 15 mg/kg on day 3 and 10 mg/kg on day 4

On enrolment a detailed history and full clinical examination will be performed and recorded on a standard Case Report Form (CRF). The patient will then be weighed. A Teflon® heparinised sampling catheter will be inserted in a forearm vein.

Baseline blood samples will be taken as described below. Part of the blood sample will be taken at baseline for immediate culture (for an in-vitro susceptibility test) and also storage of parasites

(cryopreserved in liquid nitrogen), parasite deoxyribonucleic acid [DNA] and messenger ribonucleic acid [mRNA]. On admission 5 ml blood will be collected for parasite count (thin and thick films stained by Giemsa's method), and routine biochemistry (sodium, potassium, chloride, calcium, blood urea nitrogen, creatinine, total bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, albumin, total protein, glucose and total carbon dioxide) and haematology (haematocrit, haemoglobin, white blood cell count with differentiation, platelets). An additional 5 ml of blood will be collected in a sterile heparinised tube for parasite culture and cryopreservation, and 2 ml for assessment of drug levels (artesunate and mefloquine).

The total amount of blood taken for study purposes will be 12 ml on admission and about 10 to 20 ml during follow-up (dependent on the parasite clearance time; blood collection for parasitaemia during hospitalisation will stop when the patient is parasite negative).

Sampling (2 ml):

1. Parasite counts: 0, 4, 8, 12, 18, 24 hours then 6 hourly until parasite clearance
2. Drug levels: plasma samples will be taken. Most are fixed times but for artesunate there is a population PK component so random times within time-bins are proposed. In children capillary whole blood sampling for mefloquine may need to be substituted.

Patients will remain in hospital for 7 days or longer if parasites have not cleared. They will then be followed up to Day 63 and at each weekly visit will have a haematocrit and parasite count checked.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Artesunate

Primary outcome measure

A population based pharmacokinetic-pharmacodynamic modelling approach will be used to describe the antimalarial effect of artesunate in patients with acute falciparum malaria. The objective of the modelling exercise is to characterise the relationship between pharmacokinetic variables (areas under curve [AUC], Cmax) and parasite clearance measures (parasite clearance time [PCT], parasite reduction ratio [PRR]), completed with in vitro susceptibility and molecular markers of resistance.

Secondary outcome measures

Parasitological efficacy

Overall study start date

01/01/2008

Completion date

01/06/2008

Eligibility

Key inclusion criteria

1. 40 patients with uncomplicated falciparum malaria
2. Aged greater than or equal to 15 years, either sex
3. Symptomatic of malaria infection, i.e., history of fever or presence of fever greater than 37.5°C
4. Microscopic confirmation of asexual stages of *P. falciparum* with parasitaemia greater than 10,000/ml
5. Written informed consent to participate in trial

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

40

Key exclusion criteria

1. Pregnancy or lactation (urine test for beta-human chorionic gonadotropin [β -HCG] to be performed on any woman of child bearing age unless menstruating)
2. *P. falciparum* asexual stage parasitaemia greater than or equal to 4% red blood cells (175,000 / μ l)
3. History of treatment with antimalarials (except chloroquine [CQ] or sulfadoxine-pyrimethamine [SP]) in the previous 48 hours
4. Microscopy indicates a mixed infection
5. Signs or symptoms indicative of severe malaria:
 - 5.1. Impaired consciousness (Glasgow Coma Scale [GCS] less than 15)
 - 5.2. Bleeding disorder (severe nosebleed, bleeding gums, frank haematuria, bleeding from venepuncture sites)
 - 5.3. Respiratory distress (deep breathing or respiratory rate [RR] greater than 30)
 - 5.4. Shock (circulatory collapse with systolic blood pressure [SBP] less than 80 mmHg)
 - 5.5. Hyperparasitaemia (see above)
 - 5.6. Acidosis (bicarbonate [HCO_3^-] less than 15 mmol/L)
 - 5.7. Renal insufficiency (creatinine greater than 3 mg/dL)
 - 5.8. Severe jaundice (total bilirubin greater than 2.5 mg/dL)
 - 5.9. Severe anaemia (haematocrit [Hct] less than 20% in adults or less than 15% in children)
 - 5.10. Severe hypoglycaemia (glucose less than 40 mg/dL)
6. Known hypersensitivity to artemisinin derivatives or mefloquine
7. History of convulsions or neuropsychiatric disorder
8. History of splenectomy

Date of first enrolment

01/01/2008

Date of final enrolment

01/06/2008

Locations

Countries of recruitment

Thailand

Study participating centre

Shoklo Malaria Research Unit (SMRU)

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Sponsor information

Organisation

University of Oxford (UK)

Sponsor details

Centre for Clinical Vaccinology and Tropical Medicine (CCVTM)

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Sponsor type

University/education

Website

<http://www.ccvtm.ox.ac.uk/>

ROR

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

Funder(s)

Funder type

Charity

Funder Name

The Wellcome Trust South-East Asia (SEA) Programme (Thailand)

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	30/07/2009		Yes	No