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The Africa Quinine versus Artesunate in Severe Malaria Trial

Submission date	Recruitment status	[X] Prospectively registered
22/07/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/07/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
09/05/2013	Infections and Infestations	

Plain English summary of protocol

Background and study aims.
This was the largest ever study in children hospitalized with severe malaria. It sought to determine whether a drug called artesunate was a better treatment than the usual drug quinine. Artesunate had been shown already to be superior in patients (mainly adults) studied in South-East Asia, but uncertainty remained over whether it was better in African children, who bear most of the burden of severe malaria in the world.

Who can participate?
The study was conducted in 11 centers located in 9 countries across Africa during the study period. All children hospitalized could be enrolled provided the doctor suspected severe malaria, their blood test showed malaria, they were over 18 months of age, and their parent or carer agreed.

What does the study involve?
The children were randomly allocated to receive one drug or the other by injection or by a drip. The medical staff were all aware of which treatment was given. The primary outcome of the study was whether or not the child survived to leave hospital. We also checked carefully for complications of the disease or the drug, particularly residual brain damage from cerebral malaria.

What are the possible benefits and risks of participating?
Quinine was the established time-honoured treatment. There were no risks to participating in the study and most children who were eligible were enrolled.

Where is the study run from?
The study was coordinated by the Mahidol Oxford Research Unit in Bangkok, Thailand

When is the study starting and how long is it expected to run for?
The study ran between Oct 3, 2005, and July 14, 2010

Who is funding the study?
The Wellcome Trust

Who is the main contact?
Prof NJ White
nickw@tropmedres.ac

Contact information

Type(s)
Scientific

Contact name
Prof Nicholas J White

Contact details
Faculty of Tropical Medicine
Wellcome Unit
420/6 Rajvithi Road
Bangkok
Thailand
10400
+66 (0)2 3549172
nickw@tropmedres.ac

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
076908

Study information

Scientific Title
The AQUAMAT trial: An open label randomised comparison of injectable artesunate and quinine in children with severe falciparum malaria in Africa

Acronym
AQUAMAT

Study objectives
To compare the mortality and significant sequelae of severe falciparum malaria in African children treated with parenteral quinine, to those treated with parenteral artesunate.

Please note that as of 26/01/2009 this record has been extensively updated. All updates can be found in the relevant section under the above update date. Please also note that as of 26/01

/2009 the trial dates have changed. The inital trial dates were as follows:
Initial anticipated start date: 18/07/2005
Initial anticipated end date: 31/12/2007 (amended to 30/04/2009 in February 2007)

As of 02/02/2010 the Democratic Republic of Congo was added as a country of recruitment.

As of 20/04/2010 this record was updated to include an extended anticipated end date ; the previous anticipated end date was 31/03/2010. At this time, the secondary endpoints were also updated; please see the relevant section for more details of this.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. UK: Oxford Tropical Medicine Research Ethics Committee (OXTREC) (UK), 11th August 2008 (ref: 03402)
2. The Gambia: The Gambia Government/MRC Laboratories Joint Ethics Committee, 5th October 2005 (ref: L2005.91)
3. Kenya: KEMRI National Ethics Review Committee, 21st October 2005 (ref: KEMRI/RES/7/3/1)
4. Ghana: University of Science and Technology School of Medical Science, Committee on Human Research Publication and Ethics, 23rd January 2006 (ref: CHRPE/01/06)
5. Mozambique: Ministry of Health, Comité Nacional de Bioética para a saùde, 4th June 2007 (ref: IRB 00002657-105/CNBS/07)
6. Tanzania: Ministry of Health, National Institute for Medical Research (NIMR), 20th April 2007 (ref: NIMR/HQ/R.8c/ Vol. 1/22)
7. Uganda: Mbarara University of Science and Technology, Institutional Ethical Review Committee, 22nd August 2007 (ref: Dos 1/6)
8. Nigeria: University of Ilorin Teaching Hospital, Ethical Review Committee, 26th October 2007 (ref: UITH/CAT/189/10/659)
9. Rwanda: Ministry of Health National Ethics Committee, 3rd April 2008 (ref: IRB 00001497 of IORG 0001100)

Added 02/02/2010:
10. Democratic Republic of Congo: Le Comité dEthique de lEcole de Santé Publique de l Université de Kinshasa approved on the 24th September 2009 (ref: 050/2009)

All other centres received ethics approval prior to recruiting the first participant.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

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

Interventions
Please note that as of 01/09/10 this trial has reached its target sample size and recruitment has been closed. The trial is now in follow-up.

Current information as of 26/01/2009:
Patients are randomised to treatment with either intravenous (i.v.) or intramuscular (i.m.) artesunate or i.v. or i.m. quinine.

Initial information at time of registration:
In two of the study sites intramuscular artesunate will be compared with intramuscular quinine. In two other study sites the comparison will be between intravenous artesunate and intravenous quinine.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Artesunate and quinine

Primary outcome measure
In-hospital mortality

Secondary outcome measures
Current information as of 20/04/2010:
1. Neurological sequelae at day 28 after discharge from the hospital
2. Combined in-hospital mortality and neurological sequelae at day 28 after discharge from the hospital

Initial information at time of registration:
1. Neurological sequelae
2. Recovery times:
2.1. To localise pain
2.2. To speak
2.3. To sit unsupported
2.4. To eat or breast feed, and
2.5. To discharge from hospital

Assessed at discharge.

Overall study start date
08/10/2005

Completion date
31/12/2010

Eligibility

Key inclusion criteria
1. OptiMal malaria rapid test positive, and
2. Treating physician considers patient to have severe malaria

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
5300

Key exclusion criteria
1. Patient has received more than or equal to 24 hours of effective treatment with quinine or an artemisinin derivative, or
2. Patient has a known allergy to quinine or an artemisinin derivative

Date of first enrolment
08/10/2005

Date of final enrolment
31/12/2010

Locations

Countries of recruitment
Congo, Democratic Republic

Gambia

Ghana

Kenya

Mozambique

Nigeria

Rwanda

Tanzania

Thailand

Uganda

Study participating centre
Faculty of Tropical Medicine
Bangkok
Thailand
10400

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
University Offices
Wellington Square
Oxford
England
United Kingdom
OX1 2JD

Sponsor type
University/education

Website
http://www.ox.ac.uk

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name

The Wellcome Trust (UK) (grant ref: 076908)

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 of main AQUAMAT study	13/11/2010		Yes	No
Results article	results of sub-study on malaria and HIV co-infection in Mozambique	01/10/2012		Yes	No
Results article	substudy results plasma PfHRP2	01/10/2012		Yes	No
Results article	pharmacokinetics results	01/02/2013		Yes	No