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Radical cure for vivax malaria in Indonesia

Submission date
01/05/2012

Recruitment status
No longer recruiting

Registration date
08/05/2012

Overall study status
Completed

Last Edited
25/04/2017

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Malaria is a serious tropical disease caused by a Plasmodium parasite (e.g., P. vivax and P. falciparum) spread by mosquitoes. Antimalarial medication is used to prevent and treat malaria. The current standard treatment in Indonesia for P. vivax malaria is oral artesunate combined with amodiaquine plus primaquine for 14 days. The aim of this study is to measure the effectiveness of primaquine against P. vivax malaria relapses when combined with dihydroartemisinin-piperaquine or quinine.

Who can participate?
Men aged between 18 and 60 in the Indonesian Army who have just returned from deployment at Papua and have P. vivax infection

What does the study involve?
Participants are asked to stay on the base for at least 28 days and are randomly allocated to one of the following three treatments: artesunate alone, quinine combined with primaquine, or dihydroartemisinin-piperaquine (DHA-PQP) plus primaquine. For DHA-PQP, primaquine is given 26 days after the participant finishes the DHA-PQP. The follow up lasts for one year. The participants are closely observed by doing routine tests including measurement of vital signs, blood samples, and ECG (heart rhythm) examinations. Malaria relapse rates and the effectiveness of the treatments are compared.

What are the possible benefits and risks of participating?
The findings will guide decisions about new treatments for vivax malaria globally. The main benefit is that participants are given effective drugs and are closely monitored for safety and relapse. There are two main risks in this study: drug side effects and the risk of contracting malaria. In general, these drugs are well tolerated, although in some cases side effects could occur.

Where is the study run from?
1. University of Indonesia (Indonesia)
2. Eijkman Institute (Indonesia)
3. Eijkman Oxford Clinical Research Unit (EOCRU) (Indonesia)
4. Indonesian Army Medical Corps (Indonesia)

When is the study starting and how long is it expected to run for?
November 2010 to April 2012

Who is funding the study?
1. Medicines for Malaria Venture (MMV) (Switzerland)
2. Eijkman Oxford Clinical Research Unit (EOCRU) (Indonesia)

Who is the main contact?
Prof. Inge Sutanto
sutanto.inge@yahoo.com

Contact information

Type(s)
Scientific

Contact name
Prof Inge Sutanto

Contact details
Parasitology Dept, Faculty of Medicine
University of Indonesia
Jakarta
Indonesia
10430
-
sutanto.inge@yahoo.com

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Vivax-Primaquine-ACT-QN/Oxtrec 29-10

Study information

Scientific Title
Efficacy of primaquine against Plasmodium vivax relapses when combined with dihydroartemisinin-piperaquine or quinine in Indonesian soldiers

Study objectives
The study aims to characterize the safety, tolerability, efficacy and pharmacokinetics of dihydroartemisinin-piperaquine (DHA-PQP) for the radical cure of P. vivax when combined with 14 days of primaquine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Medical Research Ethics Committee of Faculty of Medicine, University of Indonesia, 02/08/2010, ref: 328/PT02.FK/ETIK/2010
2. Oxford Tropical Research Ethics Committee, 28/09/2010
3. Clinical Trial Clearances from Indonesian FDA, 25/10/2010, ref: PN.01.06.1.31.10.10.10199

Study design
Single-center randomized open-label non-inferiority study

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Malaria

Interventions
A single center randomized open label non-inferiority study of PQ treatment against the cumulative relapse rate over 1 year when administered with two different companion blood schizontocides as radical cure of vivax malaria. Enrolled subjects were randomly assigned to one of the following arms:

1. QN+PQ = standard quinine therapy (Q™, 200 mg quinine/tablet; Kimia Pharma, Bandung, Indonesia) of 200mg base three times daily for 7 days plus concurrent dosing with 0.5mg/kg primaquine base once daily for 14 days (Malafree™; 15mg primaquine base/tablet; Shin Poon Pharmaceuticals, Seoul, South Korea)

2. DHA-PP+PQ = combined dihydroartemsinin plus piperaquine (Euartesim™, Sigma Tau, Italy; DHA-PP; 40mg dihydroartemisinin base and 320mg of piperaquine base per tablet) of three tablets for participants < 75kg, or four tablet for participants > 75kg for three days, followed by 0.5mg/kg primaquine daily for 14 days commencing on day 28 after enrollment (no safety data guided co-administration of primaquine with DHA-PP)

3. AS alone = artesunate alone (Arsuamoon™, tablet of 50mg artesunate packaged with tablet of 196mg amodiaquine hydrochloride; Guilin Pharmaceuticals Co. Ltd, Shanghai, China) was administered in a total dose of 200mg on day of enrollment, followed by a single daily dose for 6 more days

Follow up was for 365 days, counting the first day of study drug administration as Day 0.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Dihydroartemisinin-piperaquine, quinine, primaquine, artesunate, amodiaquine

Primary outcome measure
Measure and compare, using a non-inferior design, the cumulative relapse rate over one year of the two arms relative to the natural relapse rate

Secondary outcome measures
Measure the efficacy of the two primaquine combination regimens against relapse, relative to the relapse rate of the artesunate alone regimen.

Relapse efficacy is defined as:
100% x natural relapse rate - relapse rate post-PQ/natural relapse rate

Overall study start date
01/11/2010

Completion date
10/04/2012

Eligibility

Key inclusion criteria
1. Male patients between the age of 18 and 60 years
2. Traveled for >1 month to north eastern Papua within the past 12 months
3. Body weight > 40 kg and ≤ 90 kg
4. Presence of P. vivax parasitemia mono- or mixed infection with another plasmodial species confirmed by positive microscopy of P. vivax with parasite density ≥20/ µL of blood
5. Written informed consent provided by patient. If the patient was unable to write, witnessed consent was permitted
6. Glucose-6-phosphate dehydrogenase (G6PD) normal using the nicotinamide adenine dinucleotide phosphate-oxidase (NADPH) qualitative fluorescent spot test (Trinity Biologicals, USA)
7. Able to swallow oral medication
8. Able and willing to participate based on information given to patient

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
80 participants per arm, total 240 participants.

Key exclusion criteria
1. Presence of clinical condition requiring hospitalization
2. Presence of significant anaemia, as defined by Hb < 8 g/dL
3. G6PD deficient determined by a standard qualitative test
4. Definite plans for an absence of 3 days or more from the base within 28 days of being enrolled
5. Known history or evidence of clinically significant disorders:
5.1. Cardiovascular
5.2. A corrected QT interval (QTc) >450 ms*
5.3. Respiratory, including active tuberculosis
5.4. Hepatic
5.5. Renal
5.6. Gastrointestinal
5.7. Immunological
5.8. Neurological, including hearing impairment
5.9. Endocrine
5.10. Infectious
5.11. Malignancy
5.12. Psychiatric
6. Recent head trauma
7. Any other clinically significant finding that the investigator judges will place the patient at risk or interfere with the study results
8. Known to have or be confirmed:
8.1. Active Hepatitis A (e.g. by detection of anti HAV-IgM)
8.2. Hepatitis B surface antigen (HBsAg) carrier
8.3. Hepatitis C antibody (HCV Ab).
9. Liver function tests (AST/ALT levels) more than 2.5 times the upper limit of normal range
10. Renal impairment as indicated by abnormal creatinine clearance of < 60 ml/min, measured using Cockcroft-Gault formula
11. Known history of hypersensitivity, allergy or adverse reactions to piperaquine, quinine or primaquine, artesunate, dihydroartemisinin (DHA) or other artemisinins
12. Previous participation in the present clinical trial with DHA/PQP
13. Had received any investigational drug within the past 4 weeks

Date of first enrolment
01/11/2010

Date of final enrolment

10/04/2012

Locations

Countries of recruitment
Indonesia

Study participating centre
University of Indonesia
Jakarta
Indonesia
10430

Sponsor information

Organisation
Eijkman-Oxford Clinical Research Unit (Indonesia)

Sponsor details
Jl. Diponegoro No. 69
Jakarta
Indonesia
10430
+62 (0)21 391 0414
kbaird@eocru.org

Sponsor type
Hospital/treatment centre

Website
http://www.eijkman.go.id/

Funder(s)

Funder type
Research organisation

Funder Name
Medicines for Malaria Venture

Alternative Name(s)
MMV

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Switzerland

Funder Name
Eijkman-Oxford Clinical Research Unit (Indonesia)

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	01/03/2013		Yes	No