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# CYP2D6 phenotyping in vivax malaria relapsers and non-relapsers in Indonesia

**Submission date**
07/05/2014

**Recruitment status**
No longer recruiting

**Registration date**
16/05/2014

**Overall study status**
Completed

**Last Edited**
29/01/2019

**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
CYP2D6 is an enzyme found in the human body that is involved in the breakdown (metabolism) of drugs such as dextromethorphan. Some people will break down these drugs quickly while others will break them down slowly. These are referred to as different metabolizer phenotypes. If a drug is metabolized too quickly the drug may be less effective, while if the drug is metabolized too slowly there may be harmful side effects. Hence the dose of the drug may have to be adjusted to take into account the speed at which it is metabolized by CYP2D6. This study aims to find out about the possible relationship between CYP2D6 dextromethorphan metabolizer phenotype and the risk of relapse after primaquine treatment against vivax malaria.

Who can participate?
People who participated in the OXTREC 179-12 study (ISRCTN82366390) in Army Batalyon, Sragen, Central Java and who provided informed consent for genetic studies will be tested for the CYP2D6 gene.

What does the study involve?
A single dose of the over-the-counter drug dextromethorphan (DXM) for relieving cough will be given to all 26 relapsing participants and 36 randomly chosen non-relapsing participants. Based on the metabolism of that drug, which occurs exclusively through CYP2D6, we will classify the participants as fast, intermediate, or slow metabolizers.

What are the possible benefits and risks of participating?
The participants will benefit directly by knowing whether they can be successfully treated for the malarial infection or not. The drug being given is a very small dose of a common cough medicine. At this dose we expect few side effects and none being serious. There is a slight risk with taking blood from the veins. The research team will manage all risk.

When is the study starting and how long is it expected to run for?
The study will run from May to June 2014.

Where is the study run from?
This study is collaboration of the Faculty of Medicine, University of Indonesia, and Eijkman

Institute for Molecular Biology in Jakarta with Eijkman-Oxford Clinical Research Unit, Jakarta and the Indonesian Army Medical Corps.

Who is funding the study?
Medicine for Malaria Venture (MMV), Switzerland.

Who is the main contact?
Prof Rianto Setiabudy
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# Contact information

### Type(s)
Scientific

### Contact name
Prof Rianto Setiabudy

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
CYP2D6 Phenotyping/EOCRU.2014.001/OXTREC 25-14

# Study information

### Scientific Title
Case-control study of single-dose dextromethorphan CYP2D6 phenotype among patients previously dosed with primaquine and relapsing compared to those not relapsing

### Study objectives
This study aims to explore the possible relationship between CYP2D6 dextromethorphan metabolizer phenotype and risk of relapse following directly observed primaquine therapy against relapse of vivax malaria.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
1. Medical Research Ethics Committee of Faculty of Medicine, University of Indonesia, 28/04/2014, No. 244/H2.F1/ETIK/2014
2. Oxford Tropical Research Ethics Committee, 01/05/2014, Oxtrec Reference 25-14

## Study design
Open-label single-dose single-centre case-control study

## Primary study design
Interventional

## Secondary study design
Case-control study

## Study setting(s)
Other

## Study type(s)
Diagnostic

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

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

## Interventions
All subjects will be screened up to no more than 10 days prior to study drug administration and fasted overnight (minimum of 8 hours) prior to study drug administration. Subjects will receive a single oral dose of dextromethorphan 30 mg (Kimia Farma Tbk, Bandung, Indonesia) on the morning of Day 0. Serial blood and urine samples will be collected for pharmacokinetic analysis of dextromethorphan (DXM) and dextrorphan, the dextromethorphan metabolite. Subjects will be confined beginning the day prior to dosing (Day 0) and may be discharged from the study unit following the 24-hour procedures. The subjects will be discharged from the study following the completion of all end of study procedures on Day 6 ± 1 day. Total blood volume taken during the study is 120 ml (8 tablespoons).

## Intervention Type
Drug

## Phase
Not Applicable

## Drug/device/biological/vaccine name(s)
Primaquine, dextromethorphan

## Primary outcome measure

1. Pharmacokinetic parameters such as AUC0-24, AUC0-lqc, AUC0-inf, Cmax and Tmax will be estimated from plasma concentration-time data. Data from subjects prematurely ending participation in the study may be excluded from pharmacokinetic data evaluation
2. Odds ratios (ORs), 95% confidence interval (CI), and P values comparing proportions of CYP2D6 phenotype among relapsing patients compared to those not relapsing will be calculated using the Fishers exact test. The CI that included 1 and/or the P values that were >0.05 were considered insignificant

### Secondary outcome measures
N/A

### Overall study start date
15/05/2014

### Completion date
30/06/2014

## Eligibility

### Key inclusion criteria
1. 26 currently healthy subjects of OXTREC 179-12 who experienced a confirmed relapse of vivax malaria following directly observed primaquine therapy will be invited to enroll as cases in the current study
2. 36 currently healthy subjects of OXTREC 179-12 who did not experience a relapse of vivax malaria following directly observed primaquine therapy will be invited to enroll as controls in the current study
3. The subject must be able to read, understand, sign and date the IRB-approved Informed Consent Form for the current study prior to study participation
4. The subject must be judged to be in continued good health as determined by the investigator, based upon the results of a medical history, physical examination, vital signs and clinical laboratory profile
5. The subject must be able to comply with all study procedures including confinement at the investigative site and agree to participate in the entire study, returning for all visits
6. The subject must have normal clinical laboratory test results or, if abnormal, the results are not clinically significant in the investigators opinion, at Screening and on Day -1
7. Age 18 years or older, but younger than 65 years

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants

62 participants (26 relapsers and 36 non-relapsers)

### Key exclusion criteria
1. Subjects who have hypersensitivity to dextromethorphan or related compounds
2. Demonstrate a clinically significant finding from pre-treatment medical history, physical examinations, vital sign measurements, or clinical laboratory tests as determined by the investigator
3. Unwilling or unable to comply with the protocol or reside in the clinical research unit throughout the course of study
4. Has used any excluded medication, supplements or food product outlined in the protocol

### Date of first enrolment
15/05/2014

### Date of final enrolment
30/06/2014

## Locations

### Countries of recruitment
Indonesia

### Study participating centre
**Department of Pharmacology**
Jakarta
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## Sponsor information

### Organisation
ALERTAsia Foundation (Indonesia)

### Sponsor details
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### Sponsor type
Charity

### Website

http://www.alertasia.org/

**ROR**
https://ror.org/04fhhgs91

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
Medicine for Malaria Venture (Switzerland)

# 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 | 03/08/2018 | 29/01/2019 | Yes | No |