

**TCTR ID : TCTR20220317004**

Overall Recruitment Status : Completed (Has Results)

**OTHER ID :**

Prospective registration  
This protocol was registered before enrollment of the first participant.

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**Tracking Information**

First Submitted Date : 17 March 2022  
First Posted Date : 17 March 2022  
Last Update Posted Date : 03 April 2023

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**Title**

Public Title : Assessing the tolerability of a single dose of 45 mg of primaquine as an extension to assessing a potentially safer radical curative regimen of primaquine in healthy volunteers with glucose-6-phosphate dehydrogenase deficiency in Thailand  
Acronym : PQ Ascending ext  
Scientific Title : Assessing the tolerability of a single dose of 45 mg of primaquine as an extension to assessing a potentially safer radical curative regimen of primaquine in healthy volunteers with glucose-6-phosphate dehydrogenase deficiency in Thailand  
Sponsor ID/ IRB ID/ EC ID : MAL21002  
Registration Site : Thai Clinical Trials Registry  
URL : <https://www.thaiclinicaltrials.org/show/TCTR20220317004>  
Secondary ID : No Secondary ID

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**Ethics Review**

1. Board Approval : Submitted, approved  
Approval Number : TMEC 21-018  
Date of Approval : 14 June 2021  
Board Name : Ethics Committee Faculty of Tropical Medicine  
Board Affiliation : Mahidol University  
Board Contact : Business Phone : 023549100 Ext. 1349  
Business Email : [tmectropmed@mahidol.ac.th](mailto:tmectropmed@mahidol.ac.th)  
Business Address : 420/6 Ratchawithi Rd., Ratchathewi, Bangkok 10400 Thailand

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**Sponsor**

Source(s) of Monetary or Material Supports : UK MRC (MR/R015252/1)  
Study Primary Sponsor : University of Oxford  
Responsible Party : Name/Official Title : Dr. Bob Taylor  
Organization : Mahidol Oxford Tropical Medicine Research unit  
Phone : 022036333 Ext. 6373  
Email : [bob@tropmedres.ac](mailto:bob@tropmedres.ac)  
Study Secondary Sponsor : No Study Secondary Sponsor

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**Protocol Synopsis**

Protocol Synopsis : This study is an open label, single dose, one-formulation, one-period study to evaluate the pharmacokinetic (PK) and the pharmacodynamic (PD) of primaquine.

The single dose of 45 mg primaquine will be given to healthy male adult volunteers with proven G6PD deficiency. Up to 28 volunteers will be enrolled. This study will be conducted at Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University.

This study will generate valuable intra- and inter-individual data on Hb dynamics to inform the pharmacokinetic (PK), pharmacodynamic (PD) model, and provide useful evidence on the 45 mg primaquine dose recommended by WHO.

URL not available

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**Health Conditions**

Health Condition(s) or Problem(s) Studied : Malaria glucose 6 phosphate dehydrogenase deficiency

Keywords : glucose 6 phosphate dehydrogenase deficiency Primaquine Malaria

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**Eligibility**

Inclusion Criteria : 1. Male aged between the age of 18 and 65 years  
2. Hb more than and/or equal to 11 g/dL  
3. Healthy as judged by the history taking and examining physician  
4. Written informed consent provided by the volunteer. Witnessed consent is required, if the individual cannot read or write.

Gender : Male

Age Limit : Minimum : 18 Years Maximum : 65 Years

Exclusion Criteria : 1. Known to have any clinically significant disease or to have a clinically significant disease or disorder at this screening time  
2. Received a blood transfusion in the past 3 months  
3. Donated more than 300 mL of whole blood within the previous 3 months  
4. Taking or taken within the past 3 weeks any drug known to cause haemolysis in G6PD deficiency  
5. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) > 1.5 times the upper limit of normal (ULN)  
6. A serum creatinine (Scr) above the upper limit of normal (> 1.2 mg/dL) and an eGFR < 70 mL/min/1.73 m<sup>2</sup> \*  
7. Conjugated bilirubin > 1.5 x ULN  
8. Unconjugated bilirubin > 1.5 x ULN  
9. Methaemoglobin (MetHb) level > 5% determined by oximetry  
10. Have taken part in research involving an investigational drug within the past 8 weeks.  
11. Subject who is likely to be unable to follow with the study procedures

Accept Healthy Volunteers : Yes

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**Status**

Overall Recruitment Status : Completed

Key Trial Dates	Study Start Date (First enrollment) : 02 June 2022	Indicate Type : Actual
	Completion Date (Last subject, Last visit) : 29 September 2022	Indicate Type : Actual
	Study Completion Date : 29 September 2022	Indicate Type : Actual

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**Design**

Study Type : Interventional  
Primary Purpose : Health Services Research  
Study Phase : Phase 1  
Intervention Model : Single arm  
Number of Arms : 1  
Masking : Open Label  
Allocation : No Data  
Control : N/A  
Study Endpoint Classification : Safety/Efficacy Study  
Sample size  
Planned sample size : 28  
Actual sample size at study completion : 16  
Intervention Arm 1  
Intervention name : Healthy volunteer with proven G6PD deficiency  
Intervention Type : Experimental  
Intervention Classification : Drug  
Intervention Description : Primaquine 45 mg will be prescribed orally with a light snack at baseline (Day 0)

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**Outcome****Primary Outcome**

1. Outcome Name : Assess the haematological effect of a single dose of primaquine in healthy G6PD deficient hemizygous

males

Metric / Method of measurement : Haemoglobin concentrations and reticulocyte counts over time

Time point : Day 0 to Day 14

**Secondary Outcome**

1. Outcome Name : Assess tolerability

Metric / Method of measurement : Adverse events

Time point : 1 year

2. Outcome Name : Document the disposition of primaquine and carboxyprimaquine

Metric / Method of measurement : Concentrations of primaquine and carboxyprimaquine

Time point : Day 0 over 24 hour

3. Outcome Name : Define the relationships between primaquine pharmacokinetics and fall in haemoglobin and rise in reticulocyte counts

Metric / Method of measurement : Haemoglobin and reticulocyte profiles derived from a pharmacokinetic pharmacodynamic model

Time point : Day 0 to Day 14

4. Outcome Name : Attempt to identify primaquine's oxidative metabolites in blood and urine

Metric / Method of measurement : Measure 2, 3, 4 & 5 hydroxyprimaquine and 5, 6-orthoquinone in whole blood, plasma, red cells and urine.

Time point : Day 0 to Day 14

**Location**

**Section A : Central Contact**

Central Contact First Name : Bob

Middle Name :

Last Name : Taylor

Degree : MD

Phone : 022036333 Ext. : 6373

Email : bob@tropmedres.ac

Central Contact Backup First Name : Podjane

Middle Name :

Lastname : Jittmala

Degree : MD

Phone : 023548333 Ext. : No Data

Email : podjane@tropmedres.ac

**Section B Facility Information and Contact**

1. Site Name : The Clinical Therapeutics Unit, Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University

City : Bangkok

State/Province : Bangkok

Postal Code : 10400

Country : Thailand

Recruitment Status : Pending (Not yet recruiting)

**Facility Contact** First Name : Sasithon

Middle Name :

Last Name : Pukrittayakamee

Degree : MD

Phone : 023548333 Ext. : 2404

Email : yon@tropmedres.ac

**Facility Contact Backup** First Name : Podjane

Middle Name :

Last Name : Jittmala

Degree : MD

Phone : 023548333 Ext. : 2404

Email : podjane@tropmedres.ac

**Investigator Name** First Name : Sasithon

Middle Name :

Last Name : Pukrittayakamee

Degree : MD

Role : Site Sub-Investigator

**Section C : Contact for Public Queries (Responsible Person)**

First Name : Nick

Middle Name :

Last Name : White

Degree : MD, Prof

Phone : 022036333 Ext. : 6301

Email : nickw@tropmedres.ac

Postal Address : 420/6 Rajvithi road, Rajthevee

State/Province : Bangkok

Postal Code : 10400

Country : Thailand

Official Role : Study Principal Investigator

Organization Affiliation : Mahidol Oxford Tropical Medicine Research unit

**Section D : Contact for Scientific Queries (Responsible Person)**

First Name : Nick

Middle Name :

Last Name : White

Degree : MD, Prof.

Phone : 022036333 Ext. : 6301

Email : nickw@tropmedres.ac

Postal Address : 420/6 Rajvithi road, Rajthevee

State/Province : Bangkok

Postal Code : 10400

Country : Thailand

Official Role : Study Principal Investigator

Organization Affiliation : Mahidol Oxford Tropical Medicine Research unit

**Summary Results**

Date of posting of results summaries : 25 February 2023

Date of first journal publication of results : Not yet published

Baseline Characteristics : Single 45 mg dose only: Age (years): 34 (20-58) Weight (kg): 64 (52-86) Hb (g/dL): 14.0 (12.3-15.9) Reticulocyte count (%): 2.4 (1.0-2.9) Platelet count (x1000 per uL): 289 (174-412) Total WBC count (x1000 per uL): 6.6 (5.2-8.4) Methaamoglobin (%): 0.7 (0-1.4) AST (U/L): 21 (14-36) ALT (U/L): 22 (11-47) Creatinine (mg/dL): 1.0 (0.7-1.1) Total bilirubin (mg/dL): 0.7 (0.3-1.3) Haptoglobin (g/L): 1.1 (0.5-1.7) The main result is that the haemoglobin concentrations fell by a median of 1.7 g/dL (range -0.9 to -4.1; relative fall of -12% [range: -7 to -30%]).

Participant Flow : Part 1, Ascending dose 24 participants Part 2, Single 45 mg dose 16 participants

Adverse events : Haemolysis due to primaquine resulted in stopping of primaquine. Asymptomatic transaminitis probably related to primaquine. Asymptomatic transaminitis due to hepatitis E. Prolapsed intervertebral disc unrelated to primaquine.

Outcome Measures : All data analysis was done in R version 4.2.2. Haemoglobin was measured using HemoCue (daily, two samples) and using a laboratory processed complete blood count (CBC, every 4-5 days). The mean of the two HemoCue results were used in the analysis.

Brief Summary of Results : In Part 1, haemoglobin concentrations fell by a median of 3.7 g/dL (-2.1 to -5.9; relative fall of -26% [range: -15 to -40%]). Primaquine doses up to 0.87 mg/kg/day were tolerated subsequently without clinically significant further falls in haemoglobin. In Part 2, the median haemoglobin fall was 1.7 g/dL (range -0.9 to -4.1; relative fall of -12% [range: -7 to -30%]). The ascending dose primaquine regimens gave 7 times more drug but resulted in double the haemoglobin fall.

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#### Deidentified Individual Participant-level Data Sharing

Plan to share IPD : Yes

Plan description : The results of this study will be published following international guidelines and norms.

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#### Publication from this study

MEDLINE Identifier : No Data

URL link to full text publication : <https://doi.org/10.1101/2023.02.24.2328639>

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