TCTR ID : TCTR20220317004

OTHER ID :

Overall Recruitment Status : Completed **(Has Results)**

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

Tracking Information

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

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

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
	Business Address : 420/6 Ratchawithi Rd., Ratchathewi, Bangkok 10400 Thailand

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
Study Secondary Sponsor :	No Study Secondary Sponsor

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

Health Conditions

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

Keywords : glucose 6 phosphate dehydrogenase deficiency Primaquine Malaria

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 m2 *
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

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

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

Intervantion 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)

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 : Podjanee	Middle Name :	Lastname : Jittmala
	Degree : MD	Phone : 023548333 Ext. : No Data	Email : podjanee@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 : Podjanee	Middle Name :	Last Name : Jittmala
	Degree : MD	Phone : 023548333 Ext. : 2404	Email : podjanee@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 sued 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.

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.

Publication from this study

MEDLINE Identifier :	No Data
URL link to full text publication :	https://doi.org/10.1101/2023.02.24.2328639