APPENDIX 10

PARTICIPANT INFORMATION and CONSENT FORM

Study: Time-dependent pharmacokinetics of artesunate in healthy volunteers

Principal Investigators

Dr. Le Thi Diem Thuy — Cho Ray Hospital, 201B Nguyen Chi Thanh Street, District 5, Ho Chi Minh City, Vietnam

Prof. Kesara Na-Bangchang — Faculty of Allied Health Sciences, Thammasat University, Thailand

Introduction

P. falciparum malaria in Vietnam was highly resistant to chloroquine and sulfadoxine/pyrimethamine and there was increasing resistance to alternative antimalarials quinine and mefloquine. In response to the increase in resistance of malaria parasites to conventional antimalarial drugs, Vietnam has deployed artemisinin (ARN) and its derivatives with various formulations produced from locally grown *Artemisia annua* plants. Artesunate (ARS) is derived from ARN and has more potent parasite killing action than ARN. ARS has been used in treatment of malaria patients in many countries as China, Thailand and Vietnam. The establishment of a rational regimen for ARS requires more information on the pharmacokinetics of this drug. ARN has been found to have time-dependent pharmacokinetics in malaria patients and in healthy volunteers. It is not clear whether this characteristic is a common feature for all ARN derivatives. The study on time-dependent pharmacokinetics of ARS in healthy volunteers is required to answer this question. Thus, we would like to invite you to participate in this study. The study protocol has been submitted to and approved by the Ethics Committee of Cho Ray Hospital, Ho Chi Minh City, Vietnam.

Study procedure

A total of 10 healthy male Vietnamese subjects who are non-smokers and non-alcohol drinkers are planned for the study. After you have signed an informed consent form agreeing to participate in this study, you will undergo a complete evaluation to make sure that you meet all of eligibility criteria. Some screening tests may include the medical history about any chronic diseases especially for liver and kidney that you have, the physical examination, the check for your vital signs (body temperature, pulse rate, respiratory rate and blood pressure), the blood sample for routine hematology and biochemistry tests for kidney and liver functions, and the electrocardiogram (ECG) for measuring the electrical tracing of your heart. If you are suitable for the study, you will start the study soon within 2-3 days.

When you enter the study, you will receive once daily dose of 200 mg ARS (4 tablets of 50 mg ARS) in five consecutive days. After drug intake, the venous blood samples will be drawn for pharmacokinetic study, 3 ml *per* draw, at the following schedule intervals: for days 1 and 5: 6 samples will be taken at 0.5, 1, 2, 3, 4, and 6 h after drug administration; for days 2 to 4: 3 samples were taken at 1, 2, and 4 h after drug administration. The breakfast will be given 2 h after drug administration.

Benefits and Risks

You do not have any benefit in this study. ARS is a safe antimalarial drug used widely in treatment of malaria. Many scientific papers on the efficacy and safety of this drug have been published. The volume of blood taken does not harm your health.

Privacy and Confidentiality

Personal information about you will be collected for the purposes of study, but any information which can identify you will remain confidential (Helsinki declaration). Only the principal investigators and the Ethics Committee can access to your original medical records containing the identifying information to verify the data. The case report forms record you under the number and initials in the ways that can not identify the person in the report.

Reimbursement

You will not pay any expenditure in the study. Any tests that are done for research purpose will be paid by the investigator. However, you will be reimbursed some amount in VN dong for the lack of your day-work when participating in the study. If you have any injury due to the trial, you will receive the good medical care without any payment.

Termination of the study

Participation in any research study is voluntary. If you do not wish to take part, you can choose not to. If you decide to take part and later change your mind, you are free to withdraw from study at any time. Your decision not to participate or withdraw from the study will not affect anything to you, even the relationship with your doctor. Your participation can also be stopped due to the safety reason according to the decision from the doctor.

Contact persons

If you have any questions concerning this study you can contact the principal investigator, Dr. Le Thi Diem Thuy, on:

Contact number: 84-8-8551437 (ext. 153) or 0913653618

CONSENT FORM

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Principal Investigators

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Prof. Kesara Na-Bangchang	Faculty of Allied Health Sciences, Thammasat University, Thailand

I have been given clear information in Vietnamese language about this study and I have been given time to consider whether I want to take part.

I have been told about the possible benefits and risks of taking part in this study and I understand what I am being asked to do.

I have the opportunity to ask questions and I am satisfied with the answers I have received.

I know that my participation in this study is voluntary and that I can withdraw at anytime during the study without affecting my medical care.

I freely agree to participate in this study according to the conditions described in the Participant Information.

I understand that all personal information which can identify me will remain confidential.

I will be given a copy of the Participant Information and Consent Form to keep.

Participant's name: .....

Participant's signature: ..... *Date:* .....

Witness' name:* .....

Witness' signature:* ..... *Date*:* .....

** required if the participant is illiterate*

Investigator's name: .....

Investigator's signature: ..... **Date:** .....