Patient Information Sheet & ASSENT Form (10 - <18 years)

Study Title: Metformin as adjunctive therapy in overweight and obese patients with dengue: an open-label safety and tolerability trial

Short Title: Metformin in **D**engue with **O**besity (MeDO)

OxTREC reference number: OxTREC 36-19

Please read the following information carefully. You are free to ask any questions you want to make sure you are comfortable with participating. Contact details are found at the end of this document.

Introduction

You are invited into this study because your doctor suspects that you might have dengue.

Dengue is a disease caused by a virus (a very tiny organism) that is transmitted between humans through the mosquitoes' bites. The disease symptoms can range from very mild illness, which is hardly noticeable, to more significant symptoms, including high fever, headache, nausea, rash and joint pain. In a small proportion of patients, dengue can cause severe complications such as bleeding, blood clotting problems, and leaky blood vessels that may threaten patients' life. There is a suggestion that over-weight/obese patients are more likely to have severe disease compared to non-obese patients. This may make the management of dengue in over-weight/obese patients more complicated than that of non-obese individuals.

In addition, currently there are no specific drugs or effective vaccines available for dengue. Metformin is a common drug that is widely used to treat diabetes; however recent studies have shown they have additional benefits in infectious illnesses, such as tuberculosis, hepatitis C and dengue. Metformin is generally a safe medication in both adults and children, with very low risk of reduction in blood glucose level and other serious side effects. In addition, this drug also shows benefits on weight in people with obesity. In this study, we hope to learn whether metformin is safe and effective to treat over-weight/obese patients with dengue.

What will happen if I participate in the study?

Whether or not you join the study, you will receive the standard treatment for dengue according to the guidelines. Being in this study:

- You will be visited every day by a study doctor to check and record your health status until your temperature settles and you have recovered fully. You will need to stay in the hospital for at least 5 days (beginning today).
- A small blood sample (about half of teaspoonfull) will be taken for testing the liver and kidney function. The pregnancy test will also be performed in the urine samples of all female patients. These tests will help the doctors decide whether it would be safe to give you metformin.
- If you are eligible for treatment, the first dose of metformin will be given orally with a light snack. Three additional blood samples (about one and a half of teaspoonful) for testing the

blood cells and for measuring your body's responses to the virus infection will be taken before you take drug.

- If you are not eligible for starting treatment with metformin. All study procedures will then be stopped and you will receive the standard care for your illness.
- Each day you will have a small blood sample taken before the time you take drug to monitor your health and to learn about how the drug works. It's about one and half teaspoon of blood will be taken at the same time of taking blood for the hospital routine tests.
- You will receive one up to three tablets of metformin every day, based on your weight, for up to 5 days.
- You will also have an ultrasound scan of your chest and abdomen to check if there are any signs of leaky blood vessels.
- According to the standard care for a dengue patient, after your fever settles and provided your general status fits to discharge criteria, the daily assessments and blood tests will stop. However, around three to four weeks after you had fever, we would like to see you for another visit, to check that all is well. At this time we would like to take two more blood samples (one and half teaspoon) to confirm the diagnosis and to better understand how severe the infection has been.
- We also wish to store your samples for further tests, including genetic tests, which might be done at some point in the future and may be done in or outside Vietnam.

What are the possible risks of the study?

There are very few risks to you being in our study:

- The most common side effects of metformin are digestive problems such as diarrhea and vomiting. However, there are very few risks to taking the short course of metformin that we are used in this study. Metformin may cause reduction in your blood glucose level and another severe condition called lactic acidosis, which results from a buildup of lactic acid. These effects are very rare but are potentially serious, however we will watch you very carefully and check blood tests regularly, including daily glucose and lactate levels, so that we can stop the tablets if there is any problem.
- Taking blood may hurt for a short time, and may leave a bruise.
- Ultrasound scans will also be done, you may feel uncomfortable while staying still for the scan images but these scans are not painful and can be helpful to your doctor in making decisions about your care.

What are the possible benefits and compensation of the study?

You may benefit from being closely monitored by experienced doctors and nurses during the course of treatment. Tests required by the study are helpful in following up and treating your illness.

Your hospital costs for treatment and tests will be covered by the study from enrolment until discharge, and for any study related procedures or visits.

When you return to the hospital for scheduled follow-up visits, we will reimburse you a travel fee (presented to your parent/guardian).

Do I have to participate?

Your participation is completely voluntary. If you do not want to be in the study or if at any time during the study you decide to stop participating, the doctors will respect your decision. In both cases you will receive standard medical treatment.

If you decide at any time to stop participating in the study, your parent only need to inform the doctor of your decision. No new information will be collected.

Will anyone know that I am participating in this study?

In this study we will collect medical information about you. However, we assure you that all information about you will be kept confidential – the information will only be identified by a code number and we will not use your name or let anyone know who you are. This information will be kept in a safe place where only project staff can access it. Your medical records will be reviewed in strict confidence by those who are working on this study and may also be reviewed by the ethics committees and health authorities reviewing the study.

Results from this work will be published in due course in articles and medical journals, and/or may be placed on the internet, but no one will know whose information it is and you will not be identifiable.

What if I have more questions?

- You are encouraged to ask any questions related to this study during the time of participation. If you have any questions about this program, its procedures, risks and benefits, or alternatives please call Dr. Dong Thi Hoai Tam at 0918 141 641.
- If you have any questions about your rights as a subject in this study, and want to speak to someone outside of the program you may contact the OUCRU Clinical Trial Unit at +84 3924 1983.

Thank you for your time and your consideration to participate in this study.

INFORMED ASSENT FORM

To be signed by all participants aged 10- <18 years.

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SCREENING ID: [__|__]-[__|__|__]

- I have read the information given to me. I also have had a chance to discuss it with the study staff.
- I have been told about the risks and benefits. I got answers that I could understand to all my questions.
- I understand that I can withdraw from the study at any time and it will not affect my future care. If I decide to stop the study, I agree that the information collected up to the point when I stop, may continue to be used.

☐ YES or ☐ NO I AGREE to take part in the study

Participant:

By signing my name here, I confirm what is written above and that I have a copy of this form to keep until my part in the study ends.

x_____ Participant Signature/Finger print	x_____ Name	___/____/_____ Date of Signature

Investigator/Designee:

I, the undersigned, have fully explained the relevant information of this study to the person named above and will provide her/him with a copy of this signed and dated informed consent form.

x_____ Investigator/Designee's Signature	x_____ Investigator/Designee's Name	____/____/_____ Date of Signature