This study is conducted by Vietnam National TB Programme and IRD VN, who collaborate to implement this study, with support from the Institute of Tropical Medicine Antwerp in Belgium.

Part I. Patient Information Sheet BPaL-M/Lf regimens

Title of Study: Safety and effectiveness of a 6-month all-oral treatment regimen for the treatment of rifampicin-resistant tuberculosis in Vietnam

Research Assistant (RA):

Madam/ Sir,

You are being invited to take part in a study, described in this information sheet. This study is being conducted at _____. Before you decide to take part in this study, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with relatives, friends, and your doctor if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to participate or not. Your participation in this study is **entirely voluntary**. This means you will take part in the study if you want to or decide to do so out of your own choice. **You do not have to be in this study if you do not want to**. Even if you decide to participate in this study, you may **withdraw (take back your decision to participate) from this study at any time during the study**. **Your refusal to participate or withdrawal will not affect any medical or health benefits.**

Ethical approval for this study was obtained from the Ethics Committee of National Lung hospital, Vietnam, the Institute of Tropical Medicine Antwerp and Ghent University, Belgium. This study will be conducted in accordance with the ethical guidelines and principles of the International Declaration of Helsinki, as well as local ethical guidelines.

What is the purpose of this study?

As you may know, tuberculosis or TB is treatable; however, some TB bacteria stop responding to commonly used anti-TB medicines, and this is called drug-resistant TB (DR-TB), like in your case. Thus, treatment of DR-TB takes longer and causes more side effects with less chance of cure. Therefore, new TB drugs and novel regimens are urgently required to enable faster, safer and better treatment for persons with drug-resistant TB. A new shorter regimen for only 6 months with less drugs has been recommended by the World Health Organization. It has been found to work well, and the side effects were manageable. The purpose of this study is to evaluate the ability of this short regimens to kill TB bacteria and the safety of this regimen in DR-TB patients in Vietnam. We will study two regimens (so called BPaL-M and BPaL-Lf regimens). Both will last 6 months, but there is a difference in one out of 4 drugs between 2 regimens. However, both drugs used are good-working anti-TB drugs and are highly recommended by the World Health Organization for the treatment of DR-TB. The choice of the treatment regimen will be made by chance. This study will be conducted at 06 sites (provinces) in the country and only include patients ≥ 15 years.

Why was I invited to participate?

You have been selected to participate in this study because you are an adult who has been diagnosed with rifampicin-resistant tuberculosis and are eligible for treatment.

What will happen to me if I participate?

If you agree to be part of the study, you will sign a consent form and an identification number will be assigned to you. None of the information in the database will be identified with your name, but only with the code that will be assigned to you if you agree to participate, in order to maintain confidentiality. When information from your medical file is required, the medical file will only be

consulted by the medical and research team, otherwise it will be kept securely in a locked space. Your name will never be used in any reports or communications related to the study (including publication of results).

Blood and sputum samples will be tested in Vietnam for follow-up of your illness. Blood samples will not be stored. We would like to store culture-positive samples (when the bacteria in the sputum grow) for future research on tuberculosis for at least 2 years and 5 years maximum. If future research would be done, it will need to be approved by Ethics Committees. Your sputum will not be sold. If you decide that you do not want us to store your sputum sample, you can still participate in the study. Your consent form will be kept separately and securely.

As there is a possibility that your illness may reappear after treatment, you will also be asked to come for follow-up medical visits at 6 and 12 months after recovery. This will help to detect a possible recurrence of the disease and appropriate clinical measures will be taken by the medical team based on the results.

The choice of treatment regimen is determined by chance. All patients diagnosed in the same month will be on the same treatment regimen.

What do I have to do?

Before starting the treatment with the BPaL-M or BPaL-Lf regimen, we will perform a set of baseline tests, similar to patients treated with other drug-resistant TB regimens in Vietnam. The results of these tests will determine whether it is safe for you to participate in this study. In addition to the tests, we will also ask you some general questions about your health. In case you are found not eligible or do not wish to participate in the study you will be treated according to the national guidelines for drug-resistant tuberculosis.

Regardless of the choice of regimen, you must come to the RR-TB Unit in the provincial TB hospital for medical consultations and to receive medication according to the treatment protocol.

What is the most important information I should know about the BPaL-M/Lf regimen?

- The BPaL-M/Lf regimen consists of a combination of four drugs: bedaquiline, pretomanid, linezolid and moxifloxacin or levofloxacin. The last two named drugs are from the same drug family, but with minor differences. You will be assigned to either the group treated with moxifloxacin-containing regimen or the group treated with the levofloxacin-containing regimen.
- Your total participation in this study will be for 6 months, with a possibility to extend the duration of treatment to 9 months (depending on your response to the regimen). After treatment you will be contacted at 6 and 12 months to see whether you remained without TB.
- It is important to complete the full course of treatment and not skip doses. Skipping doses may decrease the strength of the treatment and your TB disease may become more resistant and very difficult to treat with other less strong TB medicines.

Before you start treatment with the BPaL-M/Lf regimen, tell your healthcare provider if:

- You had any heart problems or are taking drugs because of such problems.
- Anyone in your family has or has had a heart problem since birth (called congenital long QT syndrome).
- You have liver or kidney problems or any other medical conditions such as decreased thyroid gland function or seizures.
- You are HIV-infected. The BPaL-M/Lf regimen can also be used when HIV-infected but your doctor might need to change your ARV regimen to prevent interaction with the TB drugs.
- You are pregnant or plan to become pregnant.

- You are breastfeeding or plan to breastfeed. It is not known if the BPaL-M/Lf regimen passes into breast milk.
- You are taking any prescription and nonprescription medicines, vitamins and herbal supplements.

What will happen after the treatment has started?

- You will have to take the treatment daily under supervision at the health care facility or in the community supervised by a treatment supporter.
- If for some reason you miss a dose, inform your treatment supporter right away, and he or she will tell you what to do.
- You will also have to visit the health care center at the study site after 2 weeks and then monthly for 6 – 9 months.
- During these visits, besides physical examination, monitoring tests similar to the baseline tests will be done to see how you respond to treatment and to check for any side effects to the drugs.
- You will also have to come for follow-up visits, 6 and 12 months after finishing the treatment, for a physical examination, sputum test and chest X-ray.

What should I avoid while taking the BPaL-M/Lf regimen?

- You are advised not to drink alcohol while taking this regimen.
- It may not be safe to take some medicines or herbal products while you are on this regimen. Inform your health care provider if you are taking other medicines.

What are the possible side effects of the BPaL-M/Lf regimen?

The following are serious side effects (unwanted effects on patient's health) which have been known to occur in this study: changes in heartbeat, liver problems, nerve problems, change in vision …. but they don't happen very often, your monthly follow-up examination will ensure early detection and effective management of these side effects if any.

Other more common side effects include headache, nausea, vomiting, diarrhea, muscle/joint pain, coughing up blood, abdominal pain, chest pain, acne or rash.

It is possible that the BPaL-M/Lf regimen may also cause some problems that we are not yet aware of, hence it is important to always tell your health care provider of any side effects or health problems you experience. Sometimes because of side effects the drugs may need to be adapted or (temporarily) stopped or you can be given other medicines to decrease or prevent the symptoms of the side effect. Most of these side effects were found to be reversible. Missed doses due to safety reasons can be made up at the end of treatment. Your health care provider will advise you on this.

What are the possible risks or benefits of taking part in this study?

Risks:

All the different procedures will be carried out according to the medical protocol. There may be risks associated with your participation, but all necessary measures will be taken, and close monitoring will be carried out accordingly by the medical and research team.

Your treatment may fail. In this case, your treatment will be adjusted accordingly. Treatment failure is also possible with standard treatment. As mentioned above, you may also experience side effects, which can sometimes be serious. Your side effects will be monitored closely on a regular basis and at each visit to make sure that signs are detected early and treated accordingly.

We will ensure that your data remains confidential without identification with your name.

Benefits:

There is a greater chance that you will be cured of drug-resistant tuberculosis with the study regimens BPaL-M/Lf compared to the routinely used regimen. You will possibly be cured sooner with a shorter duration of only 6 months treatment and a lower pill burden, however this cannot be guaranteed. The information we get from this study may help us to treat future patients with drug-resistant TB better.

Do I have the right to refuse or withdraw?

You do not have to agree to take the BPaL-M /Lf regimen if you do not wish to do so. You will still have all the benefits that you would otherwise have.

If you agree to take the BPaL-M/Lf regimen, you may also at any point after you start wish to stop without losing any of your rights as a patient here. Your treatment at this health care facility will not be affected in any way. If you decide to withdraw from the study, the data about you that has been collected until your withdrawal will still be used for the analysis, without identifying your name and only for the purposes of the study, if you agree. After your withdrawal, no further analysis will be carried out on the samples you have provided us with for the study.

Also, you may be taken out of the study without your consent based on your doctor's decision. This may happen for reasons such as, your doctor feels that your continuing participation in the study may be detrimental to your health, or you do not follow doctor's instructions. Even if your participation is terminated, there would be no effect on the regular care being offered to you.

Right to access and rectify data

You have the right to ask the contact person at your clinic, who then will contact the principal investigator, to access data collected regarding care provided to you. You can ask to correct or delete data. However, once data are analysed, these analyses cannot be adapted.

Are there any associated costs and will I be paid to take part in this study?

You will be reimbursed for transportation costs that you will pay for each visit to the tuberculosis medical unit where you will have to report at the beginning of treatment and for other medical visits for the control and collection of medicines. You will also receive food support and bed fee during your hospitalization (initial enrolment or because of side effects management).

Contact person

If you have any further questions about the study or study related concerns, please contact the responsible health care provider at the study site:

Name: _____

Phone: _____

OR you can contact the principal investigator: **Nguyen Thi Mai Phuong**

Email: phuongnguyen1186@gmail.com.

Phone: 0084 949 357 999

You will receive a copy of this information sheet and the signed consent form for your records.