A Phase 2 Randomized, Open-Label Trial of PA-824-Containing Regimens versus Standard Treatment for Drug-Sensitive Sputum Smear-Positive Pulmonary Tuberculosis

NCT02256696

Informed Consent Form

28 May 2020

Participant I.D. Plate

PATIENT INFORMATION AND INFORMED CONSENT FORM

Site of Research:	**University of Cape Town Lung Institute (UCTLI), South Africa**
Protocol Title:	**A Phase 2 Randomized, Open-Label Trial of PA-824-Containing Regimens versus Standard Treatment for Drug-Sensitive Sputum Smear-Positive Pulmonary Tuberculosis**
Johns Hopkins University IRB No.:	**NA_00093014**
UCT Lung Institute Protocol No.:	**NA_00093014**
Sponsor:	**Food and Drug Administration, Office of Orphan Drug Products Development Grant Program, United States of America**
Date:	**Version No. 9.0 28 May 2020**
International Principal Investigator:	**Dr. Kelly Dooley, MD, PhD**
UCTLI Principal Investigator:	**Dr. Rodney Dawson MBChB, FCP(SA), Cert. Pulm.(SA)**

This consent form tells you about the study and the reason for doing this study. It tells you what you will be asked to do if you are in the study, and explains the things that may cause you discomfort. We may have used words that you don't understand, so please ask your study nurse or doctor if there is anything you do not understand in the consent form. You may take this consent form home to read or talk about it with your family or friends before deciding if you want to be part of this study or not.

1. What should you know about this study?

- You are being invited to join a research study. This research is sponsored by the Food and Drug Administration (FDA) in the United States of America (USA).
- The study is being carried out by University of Cape Town Lung Institute (UCTLI) in association with the Johns Hopkins University in the USA.
- This consent form explains the research study and your part in the study.
- Please read it carefully and take as much time as you need.

- Please ask questions at any time about anything you do not understand

- The word biospecimen may be used in this consent form. Biospecimen may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- A description of this clinical trial will be available on www.sanctr.gov.za as required by South African law.
- For clinical trials: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
- All your health information collected during the study will be confidentially stored and only those persons working on the study will have access. We are asking you to allow us to use and give out details about your health, including medical notes and lab results as allowed by this U.S. law (and local South African law). Your name or information that directly identifies you will not be included with your sample or with your medical information. You do not have to agree to allow us to use and give out the details. If you do not agree, you may not join this research study.
- For clinical trials: If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

This study is being run by the University of Cape Town Lung Institute.

2. Why is this research being done?

This research is being done to see if a new drug called PA-824 can improve the treatment of tuberculosis (TB).

If a drug is new, it means that it has not been approved by the United States Food and Drug Administration (FDA). The FDA is an agency of the United States Department of Health and Human Services which controls the use of medicines in the USA. PA-824 is also not registered for use in South Africa. The FDA is allowing the use of PA-824 in this study.

People joining the study will receive either PA-824 for 12 weeks with Rifampin, PA-824 for 12 weeks with Rifabutin, or standard TB treatment including ethambutol and Rifampin for 8 weeks. Everyone joining the study will also get two standard TB medicines called isoniazid (INH) for 12 weeks, and pyrazinamide (PZA) for 8 weeks. After you have been in the study for 3 months, you will receive standard TB treatment medicines from your TB clinic for 3 more months to finish your TB treatment.

In this study, PA-824 will be given at a dose of 200 mg per day.

3. Who can join this study?

- To join this study you must have TB in your lungs and your sputum test must show that you have TB. You must not have had more than five days of treatment for active TB in the past six months.
- It is important that you tell your study doctor or nurse what other medicines you are taking and have taken in the past 2 months as some medicines cannot be taken with the study

medicines. We will also need to know what other diseases you have had as some other lung diseases will prevent you from taking part in the study.

- Only participants 18 years or older can join this study.
- You must weigh between 40Kg and 80Kg.
- You must be able to care for most of your needs and understand what you need to do for this study and be able to attend the Lung Institute clinic for study visits.
- You can be HIV positive or negative, but your CD4 count must be greater than or equal to 350 cells/cu mm. You cannot be currently taking or plan to take combination antiretroviral therapy for HIV for the next three months.
- The TB medicines called Rifampicin and Rifabutin may stop birth control pills, hormone injections, and hormonal implants from working to prevent pregnancy. Therefore, while you are on this study, you must use some other kind of birth control. Not having sex is also a way to avoid pregnancy while in the study. Women who are able to have children must have a urine test for pregnancy and the test must be negative for her to join the study.
- Women who are pregnant or breastfeeding may not join the study. Women who plan to become pregnant may not join the study.
- The blood tests for this study must show the study doctor that it will be safe for you to be in the study.
- Patients who are allergic to the study TB medication may not join the study. Patients who have a disease which will be affected by the study TB medication may not take part in this study.
- Your study doctor or nurse will check to see if it is safe for you to take part in the study. Your study doctor will make sure that you are able to come to the clinic for your study visits. They will also make sure that you are able take your study TB medicine properly.
- Before you have any study visits it is important that you understand this information, and that you sign this form.

4. What happens if you do not join this study or if you decide to leave the study early?

You are a volunteer in this study. If you decide to join the study you can leave the study at any time. It is up to you to decide to join this study or not. If you decide not to be part of this study or if you leave the study early, your care at the TB clinic will not be affected in any way. If you leave the study early you will be treated for TB at your local clinic with the routine TB medicines.

If the study doctor decides it is not safe for you to join this study or you cannot join the study, your study doctor will talk to you about the best and safest treatment for your TB at this time.

If your study doctor finds that your TB can't be treated with the medicine (is resistant), the study regimen will be stopped and we will ask you to return in 7-14 days for a safety visit. You will still need to continue TB treatment with different medicines. We will advise you as to how and where you should continue with your TB treatment.

If you decide not to participate you will still need to receive routine treatment for your TB for six months. If you leave the study early you will need to receive routine medications for TB until you complete six months. We will help you with how and where you should continue with your TB medicines.

If you decide to leave the study, with your permission, we will ask you to continue your study visits. If you decided to leave the study early, we will request that you return for a final safety visit within one week.

We may learn things during the study that might make you want to stop being in the study. If this happens, we will tell you about it. You can then decide if you want to stay in the study or whether you want to take the routine TB medicines only.

5. How many participants will be in this study?

About 183 participants will be in this study.

6. What will happen if you join this study?

If you agree to be in this study and you have signed this Informed Consent Form, you will need to visit the Lung Institute clinic about 13 times over the next 12 months. You will have the following tests to make sure that you can take part in the study safely and to check that you have TB:

Screening Visit (First visit)

The following tests will be carried out to make sure you have TB and that you can take part in this study safely:

- Your medical history will be collected from your medical records and by talking to you.
- You will be asked questions about your health. These questions will include:
  - -Questions about your TB and how it makes you feel,
  - -Whether you have had past treatment for TB
  - -Any other illnesses you have had
  - -And if you drink alcohol or take drugs.

  Some of these questions are personal and you do not have to answer them if you do not want to.
- We will also ask you your age and whether you are male or female. Your heart rate, blood pressure, breathing rate and temperature will be measured. We will also measure your height and weight.
- We will ask you about any medicines you are taking now and any medications you have used during the last 14 days.
- If you are a woman, you must not be pregnant or breast-feeding. You must not become pregnant during the six months you are on treatment for your TB. This is because the study TB medication may harm an unborn child. It may harm your baby if you are breastfeeding. Women who are capable of having children will be asked to give a urine sample. This sample will be checked for pregnancy.
- Women who are able to have children will be asked about what type of birth control they are using. Rifampicin may stop birth control pills, hormone injections, and hormonal implants from working to prevent pregnancy. So, while you are on this study you must use some other kind of birth control. This could include a diaphragm or cervical cap, condom, birth control sponge, or IUD. You need to use one of these kinds of birth control instead of, or along with, birth control pills, hormone injections, or hormonal implants. Not having sex is also a way to avoid pregnancy while in the study.

- If you are a male participant who is having intercourse with women who are able to have children, there are some requirements. These must be used while you are taking part in the trial and for 12 weeks after your last dose of study medicine. These include the following:
  - Use of a male condom, diaphragm, cervical cap, or female condom; or
  - Use of one of the above with hormonal contraceptives or an intra-uterine device for the female partner.
- You will have your eyes tested to check how well you can see, including seeing colors. Your eyes will also be checked to make sure you don't have any cataracts.
- We need to know whether or not you are HIV positive. This is a recommended test for everyone with TB and is needed for this study. All participants will have an HIV test and counseling (even if you have had an HIV test before) and you will need to sign a separate consent form to confirm that you give permission to have an HIV test. This will be done at the Lung Institute Clinic with a finger prick test. Sometimes more than one test is needed. Please note the results of these tests will be kept confidential at all times.
- If you are HIV positive, you will have about another 2 teaspoons (10 ml) of blood taken from a vein for a CD4 (T-cell) count. We will give you the result of this test. We will not do the CD4 count test if we can get a written copy of this test result from anytime in the 3 months before you start the study medicines.
- We will take about another 4 teaspoons (20 ml) of blood from a vein to check your liver, kidneys, and blood count. We will also check the protein in your blood (albumin) and a salt called potassium. These tests are to make sure it is safe for you to take part in the study. You will have these blood tests before starting the study, unless we can get the results of the same tests done within the past 14 days.
- A sputum (material coughed up from the lungs and windpipe) test will be done to check if you have TB or not. Only participants who have TB can take part in this study. This sputum will be tested to make sure that the study drugs will work on your TB.
- We will also check if you have TB by doing a chest x-ray (a photograph of your lungs). If you have had an x-ray of your lungs within 14 days before your screening visit (first study visit), and we can get your results we won't need to do another x-ray.
- We will also perform an ECG. This is a simple and fast procedure to record the electrical activity of the heart. An electrode is attached to your chest, arm, and leg. The procedure does not cause pain or discomfort.

After your screening visit your study doctor will decide whether you are able to continue in the study or not. If you are not able to continue in the study we will explain why and we will help you to get the right care for your TB at a place convenient for you. If you are able to continue in the study you will need to return to the Lung Institute clinic for another study visit called the baseline visit. This visit will take place as soon as possible after the screening visit (first study visit).

Baseline Visit

At the baseline visit we will check again to make sure you can take part in this study safely. The following tests and procedures will also be carried out:

- Your heart rate, blood pressure, breathing rate and temperature will be measured. We will also measure your weight.
- We will ask you about any medications you have started taking since your screening visit.

- We will give you information on the study drug (PA-824) and the standard TB treatment drugs to make sure that you know what the side effects of these drugs can be and what to do if you have these side effects.
- We will ask you questions about your health and about your TB.
- A sputum (material coughed up from the lungs and windpipe) test will be collected.
- Women who are capable of having children will be asked if they could be pregnant and the date of the first day of their last menstrual period (monthly bleeding). If there is a chance you could be pregnant you must tell the study doctor or nurse. You may be asked to give a urine sample which will be used to check if you are pregnant or not.

Study Regimen

At your Baseline Visit, if you are able and still want to participate in the study, you will be randomly assigned (by chance, like pulling numbers from a hat) to one of 3 study groups:

1. One group will have 8 weeks of daily standard TB medicines given once a day for 7 days per week, then 4 weeks of isoniazid and rifampin.
2. One group will have 8 weeks of PA-824 at a dose of 200 mg per day plus 3 standard TB medicines given once a day for 7 days per week, then 4 weeks of PA-824, isoniazid and rifampin.
3. One group will have 8 weeks of PA-824 at the dose of 200mg per day and Rifabutin plus 2 standard TB medicines, then for the next 4 weeks PA-824, isoniazid, and Rifabutin.

The same number of people will be put onto each of the three groups.

Everyone will also take a 50mg Vitamin B6 tablet with each dose of TB medicines. This decreases the chance of a numb feeling in the arms and legs when taking TB medicines.

All of these medicines are tablets which you will need to swallow.

Taking the Study Medicines:

Your TB medication will be given to you each day by study team member or a health care worker. Your treatment might also be given to you by a lay treatment supervisor, family member or employer. Anyone who gives you medicine will have received training about the study. This way of giving you your TB treatment is called 'Directly Observed Therapy' (DOT) and this will happen for the first 12 weeks of you taking TB medication. You may take your TB medication at the TB clinic or other health care facility. If you prefer, you may take the medication at your home or work. The reason for this is because we have to make sure that each participant on this study takes their medication properly.

Depending on which group you are in, you will be told whether or not your study medicines should be taken with food.

In this study, you cannot take certain medicines during the first 3 months of taking the TB medicines. This includes medicines to treat HIV infection. The study team will discuss all medicines that you are taking to make sure that there are no problems.

How long will you be in the study?

- You will be in the study for 12 months in total. You will take TB study medicines for the first 3 months (12 weeks) and then standard TB treatment for the next 3 months (12 weeks). You will have to return to the Lung Institute clinic weekly for the first 8 weeks and then weeks 10 and 12. You will also be asked to return to the Lung Institute for follow-up visits at month 4, month 6 and month 12.

Weekly Study Visits (Weeks 1, 2, 3, 4, 6, 8, 10, 12)

You will have frequent study visits to the Lung Institute clinic for the first eight weeks of the study. Your first visit will be Day 7, the day of your 7th dose.

The following tests and procedures will be done during these weekly visits:

- You will meet with a study doctor or nurse every week after you start the study for 8 weeks. These study visits will take about 30 minutes.
- You will be asked questions about your TB, how you are feeling and if you have taken any medicines or had any illnesses since your last Lung Institute clinic visit. We will also ask you if you have taken any new medicines (over the counter and prescription medicines) since your last visit.
- We will measure your heart rate, blood pressure respiratory rate, temperature and weight.
- We will also perform an ECG at weeks 1 and weeks 4. If you are withdrawn early from the study you will also need an ECG. This is a simple and fast procedure to record the electrical activity of the heart. An electrode is attached to your chest, arm, and leg. The procedure does not cause pain or discomfort
- You will have blood taken from a vein at your Lung Institute clinic visit at weeks 1, 2, 4, 6, 8 and 12, to check your liver, kidneys, and blood count. At week 3, blood will be taken to check your liver. If you are withdrawn early from the study you will also need to have blood taken at that visit. We will take about 2 teaspoons (10 ml) of blood for these tests. These tests will help us to decide if it is still safe for you to be in this study.
- We will give you information on the study drug (PA-824) and the standard TB treatment drugs to make sure that you know what the side effects of these drugs can be and what to do if you have these side effects.
- A sputum (material coughed up from the lungs and windpipe) test will be done at each of the weekly study visits. This test is important in this study as it will tell us how well the study drugs are working.
- At your 4 week Lung Institute clinic visit you will have your eyes tested again to check how well you can see and how well you can see different colours.
- Women who are capable of having children will be asked if they could be pregnant and the date of the first day of their last menstrual period (monthly bleeding). If there is a chance you could be pregnant you must tell the study doctor or nurse. You may be asked to give a urine sample which will be used to check if you are pregnant or not.
- Two weeks after you start the study, we will measure the level of the study drug in your blood. You will need to stay at the clinic until 8 hours after you have taken your study TB medicines. You will have a needle put into a vein. We will take less than 1 teaspoon (4 ml) of blood 5 times on this day for a total of 5 teaspoons. The next morning you will need to come to the clinic before you have taken your study TB medication so that we can take another 1 teaspoon (4 ml) of blood for the PK test.
- Three other times in the study (at Weeks 4, 8 and 12), we will ask for two blood samples to

test the level of the study drug in your blood. If you are withdrawn early from the study you will need to come to the clinic so that we can take another 1 teaspoon (4 ml) of blood for this test.

If you are taking the regular TB medicines, you will not have the extra blood samples (PK testing) taken.

Follow-up Study Visits:
This part of the study starts when you finish taking the study TB medicines (after the first 3 months on the study). Your TB treatment will continue until you have had a total of 6 months of TB treatment. You will collect this medication at your TB clinic to which we will refer you when you have completed study medication. During this part of follow-up, you will receive standard, routinely used TB medicines. In most cases this will be isoniazid and rifampicin, which are the usual medicines used to finish TB treatment. To be cured, it is essential that you complete your full course of TB treatment.

In some instances, the TB doctors may want to treat you for longer than 6 months. They will discuss this with you if this needs to happen.

Month 4 Follow-up Visit
You will also have a study visit at month 4. This visit will take about 15 minutes and will include:

- You will be asked questions about your TB and how you are feeling and if you have taken any medicines or had any illnesses since your last Lung Institute clinic visit.
- You will be weighed.
- We will give you information on the standard TB treatment drugs to make sure that you know what the side effects of these drugs can be and what to do if you have these side effects. We will also check to see how you are taking your TB medication.
- A sputum (material coughed up from the lungs and windpipe) test will be done to see if the TB is responding to treatment.

Month 6 Follow-up Visit
After 6 months you will meet with a study doctor to discuss your TB and how you are feeling. The doctor will also ask you about medicines you have taken and if you have been sick.

- You will be weighed.
- We will check to see how you were taking your TB medication.
- You will have your eyes tested to check how well you can see and how well you can see different colours and to make sure you don't have any cataracts.
- A sputum (material coughed up from the lungs and windpipe) test will be done to see if the TB is responding to treatment.

Months 12 Follow-up Visit
At month 12 you will meet with a study doctor or nurse, or be contacted on the phone. This will take about 15 minutes and will include:

- You will be asked questions about your TB and how you are feeling and if you have taken any medicines or had any illnesses since your last Lung Institute clinic visit.

7. What are the risks or discomforts of the study?

All medicines have possible side effects. Some medicines should not be taken with TB medicines. You should tell the study nurse or doctor about all the medicine you are taking. You should talk with them before you start any new medicine during your TB treatment. It is possible that the study TB medicine which we are studying may not be as effective as the standard TB medicines.

Some of the medicines used in this study have been linked with liver problems and could be harmful to it. These medicines are:

pyrazinamide,
isoniazid,
PA-824,
Rifabutin, and
rifampicin.

A few people in another study got liver problems and they died. Liver problems are common in patients taking TB medicines. In patients taking normal TB treatment about 5 out of 100 patients may develop liver problems. In this study, we combine a new drug with routine TB medication. This may put you at a higher risk for liver problems. Liver problems cause nausea or vomiting, stomach pain, fever, weakness, itching, unusual tiredness, loss of appetite, light coloured bowel movements, dark coloured urine, yellowing of your skin or the white of your eyes. Liver problems may show up in your blood. In rare cases liver problems may be serious and even lead to death. Extra laboratory tests have been added to watch your liver health more closely. Please talk to your study doctor about any worries you have about this. Talking to your doctor is important if you have had liver problems before. It is also important if you drink alcohol or use herbal medicines.

The study drug may hurt your liver. Liver harm can be seen in the blood. Liver harm in your blood is possible if you are taking other medicines that affect your liver. We will check your blood frequently to check for liver harm.

Side Effects of PA-824:

Common side effects (1-10%)

- Headache
- Skin rashes
- Stomach cramping
- Swelling of the liver, called hepatitis. If you have this swelling, you might notice yellow eyes, very poor appetite, nausea, vomiting, or pain in the right side of your abdomen.
- Some people in other studies have had a high kidney level in their blood.
- Some people in other studies had a mild change in their heart rhythm.

Rare, but serious side effects (less than 1%)

- It is possible that the study drug may affect male reproductive organs. It is also possible that both men and women could get cloudy eyes. Also, this drug has caused one person to fit. You will be checked for fitting during the study.

Side Effects of Standard TB medicines:

Common side effects (5-10%)

- Upset stomach, poor appetite, nausea, vomiting, diarrhea, headache
- Joint pains
- Mild, itchy skin rash
- One of the TB medicines can make your tears, sweat, saliva, faeces, and urine turn orange. Contact lenses may be stained permanently due to the orange colour of your tears.

Rare, but serious side effects (less than 1%)

- Loss of vision. Loss of vision may last for a short time or be permanent. We will check your vision before you start the study and again at your week 4 visit.
- Uveitis or inflammation of the uvea in the eye is, you might notice redness of the eye or blurred vision.
- Liver swelling called "hepatitis". You might notice yellow eyes, very poor appetite, nausea, vomiting, or pain in the right side of your abdomen.
- One of the routine TB medicines can cause seizures or trouble thinking.
- Allergic reaction (rash and fever) to any of the standard TB medicines is possible. Rarely, an allergic reaction can cause low blood cell counts or kidney damage.

There may be other side effects from these medicines that we don't know about yet. If you have side effects, you must tell your study doctor or nurse right away. If you do have side effects your study doctor or nurse will explain to you how to carry on taking your TB medicines. For serious side effects, you might have some blood tests. You may be taken off the study medicine for safety reasons. Your study doctor will then decide what treatment is best for you.

Blood Taking: There are a few small risks from having blood taken from a vein or from having your finger pricked. These include brief pain from the needle stick or finger prick, bruising, bleeding, dizziness, and only in very few patients, infection where the needle enters the vein or where your finger is pricked. These same risks are true for the "butterfly" or "cannula" used for the frequent blood draws for the pharmacokinetic (PK) testing.

Sputum Test: Some people find this test uncomfortable.

Urine Test: There is no risk from urinating. You will be asked to do this privately.

ECG Test: There is no pain or discomfort from this test. An electrode is attached to your chest, arm, and leg.

Eye Test: The slit-lamp is a low-power microscope combined with a high-intensity light source. The health care provider will examine your eyes. Often a yellow dye (fluorescein) is used to help examine the cornea and tear layer. The dye rinses out of the eye with tears as you blink. Your eyes will be sensitive to light for a few hours after the exam if dilating drops are used.

Risks of Radiation from X-ray: X-rays are routinely used to diagnosis TB. You will have an x-ray when you start the study unless you had one in the previous 14 days. X-rays include exposure to radiation from x-rays or gamma rays. X-rays and gamma rays can damage cells, but at low doses, the body is usually able to repair these cells.

The radiation exposure that you will get in this research study is 0.01 rem (a rem is a unit of absorbed radiation). This is less than the 0.3 rem that the average person in the United States gets

each year from natural sources like the sun, outer space, air, food, and soil. The risk from the radiation exposure in this research study is very small.

HIV test: HIV testing includes counseling before and after the test. You will be told the test result. You will be told the meaning of the test result, whether it is positive or negative. Some people who have an HIV test might feel anxious. If you feel this way, you can talk about it with Dr. Rod Dawson, Tel: 021 406 6856, Cell: 083 2907322. We will keep your HIV test results private as much as the law allows, but there is a small risk of loss of confidentiality about HIV test results.

8. Are there risks related to pregnancy?

We do not know enough about the safety of the study medicine, PA-824 when taken by pregnant women or women who are breastfeeding. Therefore, you will not be allowed to take part in this study if you are pregnant, plan to become pregnant during TB treatment, or if you are breastfeeding.

If you can get pregnant, you will have a pregnancy test (a urine test) before starting this study. The test must be negative before you can start this study.

Two of the medicines for TB may stop birth control pills, hormone injections, and hormonal implants from working for the prevention of pregnancy. Therefore, while you are in the study, you must use some other kind of birth control. Not having sex is also a way to avoid pregnancy while in the study.

If you become pregnant during the study, you must tell the study doctor or nurse right away. The study medication will then be stopped. We would like to ask you questions about your pregnancy history as well as information about the current pregnancy and birth. We would also like to follow the health of your infant for six months. If you do become pregnant, your doctor will decide what TB treatment is best for you.

If you are a male and your female partner becomes pregnant, we would like to ask permission of your partner to collect information about her pregnancy history as well as information about the current pregnancy and birth. We would also like to follow the health of the infant for six months.

9. Are there benefits to being in the study?

There may or may not be a benefit to you from taking part in this study. By taking part in this research you may help us find out if PA-824 can improve TB treatment for other patients with TB in the future.

10. Will it cost you anything to be in this study?

There is no cost to you for being in the study. You will not have to pay for any medicine or tests that are part of this study.

11. Will you be paid if you join this study?

You will not be paid for taking part in this study. However, you will be reimbursed for your time and the cost of coming to the Lung Institute clinic visit. For each scheduled study visit at the clinic, you will receive R300. If you need to have the PK blood testing about 14 days after

starting the study, you will need to stay at the Lung Institute Clinic until 8 hours after you have taken your study TB medicines and you will receive R450 for your time and inconvenience. If you are asked by the site team to come for an unscheduled study visit at the clinic, you will receive R150.

12. Leaving the study early

The study doctor may take you out of the study early if they think you are not getting better on the study or if you have a bad reaction to the study medicines. They may also take you out early if you need other medicine that is not allowed on the study. If you do not come to the clinic or take the study medicines the doctor will take you out of the study. The study might be cancelled and end early. Also, you may leave the study early if you wish.

Even if the study medicines are stopped, we may still follow you in the study for a total time of 12 months.

13. How will your privacy be protected?

This study is being done by the FDA (Food and Drug Administration) in the United States.. There is a privacy law in the United States that protects the health information that you give us. There is also a privacy law in South Africa that protects this information. These laws says that health information may only be used under strict rules. We will ask you to give us details about your health as part of this study. These details have been listed on this form.

The study team may see the details about your health. Also, some United States government officials and groups (such as the Food and Drug Administration), members of the Ethics Committee/s who have approved this study and members of the South African Health Products Regulatory Authority (previously known as the Medicines Control Council), or other companies that have given money to do the study may see details about your health.

We are asking you to allow us to use and give out details about your health. All of your health information collected during the study will be confidentially stored and only those persons working on the study will have access. Also, your name and information that identifies you, will not be included with your medical information. Your information and tests will be stored to keep your identity from being known. You do not have to agree to allow us to use and give out the details. If you do not agree, you may not join this research study.

If you agree to allow us to use and give out the details about your health, you can decide later to change your mind. If you change your mind, please tell us in writing or ask the study team to write down for you this decision to change your mind. From that date on, we will not collect new details about your health and will only use the information or samples collected up to that date.

The study findings may be published in a report so that others can know the study results. The report will not contain your name or other information that could be used to identify you.

14. Will the study require any of your other health care providers to share your health information with your study doctor or nurse?

Your study doctor may ask to see your health information from your other doctors.

With your permission, we will ask these other doctors to give us information about your health or your health care involving tuberculosis. We may also ask for your CD4 count if you have already had this test.

In South Africa it is the law that we must report your TB to the TB clinic.

15. What happens if I am injured because of taking part in this study?

If you are injured as a result of being in this study, you will be given immediate treatment for your injuries. They will also refer you to another healthcare provider for further care if you need it.

There is no programme for compensation through the study sponsor (Johns Hopkins), however, this research study is covered by an insurance policy taken out by the University of Cape Town if you suffer a bodily injury because you are taking part in the study.
The insurer will pay for all reasonable medical costs required to treat your bodily injury, according to the SA Good Clinical Practice Guidelines 2006 (or latest version), which are based on the Association of the British Pharmaceutical Industry Guidelines. The insurer will pay without you having to prove that the research was responsible for your bodily injury. You may ask the study doctor for a copy of these guidelines.

The insurer will not pay for harm if, during the study, you:

- Use medicines or other substances that are not allowed
- Do not follow the study doctor's instructions
- Do not tell the study doctor that you have a bad side effect from the study medicine
- Do not take reasonable care of yourself and your study medicine

If you are harmed and the insurer pays for the necessary medical costs, usually you will be asked to accept that insurance payment as full settlement of the claim for medical costs. However, accepting this offer of insurance cover does not mean you give up your right to make a separate claim for other losses based on negligence, in a South African court.

It is important to follow the study doctor's instructions and to report straightaway if you have a side effect from the study medicine.

16. What other things should you know about this research study?

What is the Institutional Review Board (IRB) and how does it protect you?
This research study has been approved by both the Johns Hopkins Medicine IRB in the United States of America. It has also been approved by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (UCTHREC) in South Africa.

The Johns Hopkins Medicine IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant. You may also contact them if you think you have not been treated fairly. The IRB office number is +1 410-955-3008. You may also call this number for other questions, concerns or complaints about the research. The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The University of Cape Town Faculty of Health Sciences Human Research Ethics Committee's purpose is to review human research studies. It also protects the rights and welfare of the people participating in those studies. You may contact the UCTHREC if you have questions about your rights as a participant in this study or if you think you have not been treated fairly. The UCTHREC's telephone number (Professor Marc Blockman) is (021) 406 6338.

The study doctor has no conflict of interest enrolling you as a participant in the study.

What do you do if you have questions about the study?
You can phone the International Principal Investigator for this study, Dr. Kelly Dooley (+1 443-287-0517), at Johns Hopkins in Baltimore, Maryland USA, or you can call the Principal Investigator at the Lung Institute, Dr. Rod Dawson (Tel: 021 406 6856, Cell: 083 290 7322).

If you cannot reach the Principal Investigator or you want to talk to someone else, you can phone the Human Research Ethics Committee (UCTHREC) Tel: 021 406 6338. An Ethics Committee is an independent committee to help protect the rights of research participants.

After you have spoken with your doctor or the Ethics Committee and if they have not provided you with answers you need, you should write to the South African Health Products Regulatory Authority (SAHPRA) at:
The Chief Executive Officer
South African Health Products Regulatory Authority (SAHPRA)
Department of Health
Private Bag X828
Pretoria
0001
E-mail: enquiries@sahpra.org.za
Website: https://www.sahpra.org.za

What should you do if you are injured or ill as a result of being in this study?
Phone Dr. Rod Dawson, Tel: 021 406 6856, Cell: 083 290 7322, if you have an urgent medical problem related to your taking part in this study.

What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

None of your biospecimens will be stored for future use or research beyond the study.

17. What does your signature on this consent form mean?

Your signature on this form means that:

- you understand the information given to you in this form
- you accept what is written in this form
- you agree to join the study
- You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Printed name of subject	Signature of subject	Date/Time
Printed name of person conducting Informed consent discussion	Signature of person conducting Informed consent discussion	Date/Time
Printed name of Investigator	Signature of Investigator	Date/Time
Printed name of witness (if required)	Signature of witness (if required)	Date/Time

NOTE: **A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; AND, IF APPROPRIATE A COPY OF THE CONSENT FORM MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD.**