

PARTICIPANT INFORMATION LEAFLET AND INFORMED CONSENT FOR PARTICIPANTS (> 18 YEARS) WHO ARE PREGNANT

STUDY NUMBER: BEAT Tuberculosis (Building Evidence for Advancing new Treatment for Tuberculosis)

STUDY TITLE: An open label, randomized controlled trial to establish the efficacy and safety of a Study Strategy consisting of 6 months of bedaquiline (BDQ), delamanid (DLM), and linezolid (LNZ), with levofloxacin (LVX) and clofazimine (CFZ) compared to the current South African Standard of Care (Control Strategy) for 9 months for the treatment of rifampicin resistant tuberculosis (RR-TB)

SPONSOR: USAID (United States Agency for International Development)

PRINCIPAL INVESTIGATOR: Dr Francesca Conradie

INSTITUTION: Isango Lethemba TB Research Unit

DAYTIME AND AFTER HOURS TELEPHONE NUMBER(S): _____

To the potential participant: This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

1. Introduction

Good day, my name is _____. I am a _____ at the Isango Lethemba TB Research Unit.

You are being asked to sign this additional informed consent form because you have already given consent to take part in the BEAT Tuberculosis trial and it has been confirmed that you are currently pregnant.

There is very little evidence on what the best medicines are to treat pregnant females who have drug resistant TB. In South Africa, pregnant females with this type of TB at all stages of pregnancy are given the same medicines as people who are not pregnant. It is therefore important to learn more about how these medicines work during pregnancy. This study allows us to collect very important information on how the TB medicines work in pregnancy and to watch you closely.

There is also very little known about how much of the TB medicines are in breast milk and how this affects the baby.

2. Procedures

- A scan will be done as soon as your pregnancy is confirmed, to check that everything is okay with your pregnancy.
- A scan will be done between week 16 and week 20 of your pregnancy to check that your baby is healthy. If you are already past this stage in your pregnancy when you inform your study doctor, a scan will be done immediately.

3. Risks

TB is a serious illness that can be fatal. The combinations of medicines used to treat TB have rarely been associated with serious side effects including death. Regular checkups are done to look out for any other side effects. To the best of our knowledge, none of the current TB medicines produce problems in pregnancy, however we cannot guarantee that the medicines you are taking in either treatment strategy, will not affect your baby.

4. Additional optional pregnancy PK sub-study (if you are still on TB medicines at the time your pregnancy is confirmed)

This sub-study is for all pregnant females, 18 years of age or older on both treatment strategies. Participants must be taking their TB medicines at the time of these sub-study visits. If you agree to take part in this sub-study, we would like to take blood from you and your baby at different visits during the study.

During the third trimester of your pregnancy (this is when you are more than 28 weeks pregnant):

At any visit during your third trimester, blood will be drawn 6 times over 24 hours. These time points are: before you take your dose of TB medication (pre-dose) and then 2, 4, 6, 8, and 24 hours after you have taken your dose of bedaquiline, clofazimine and levofloxacin (post-dose).

Approximately one teaspoon of blood will be taken with each blood draw (about 6 teaspoons or 30 milliliters in total). The blood will be taken from you by inserting a small plastic tube into a vein in your arm, which will remain there for the full 24 hours. Blood will be drawn from the tube so that you do not need to be pricked with a needle every time blood is drawn. After the blood sampling is finished, the tube will be removed and the site will be covered with a plaster to prevent unnecessary bleeding.

- Before the PK visit: Please do not take any of your study medicines on the morning of your scheduled PK visit. Bring all of your medicine to the research unit. The study staff needs to give you the dose at a very specific time at this visit. It is very important that you take all of the TB medication doses, as directed by the study staff, for the full duration of your TB treatment.
- What will happen at the PK visit: A small plastic tube (like a “drip”) will be placed in your arm to draw blood samples at: pre-dose and then 2, 4, 6, 8, and 24 hours after you have taken your dose of bedaquiline, clofazimine and levofloxacin (post-dose).

You may be required to stay overnight at the clinic for the PK sub-study. After the 8 hour blood draw of the PK sub-study visit, you may leave the clinic if the study doctor or study staff believes it is safe for you to do so and return for the 24 hour blood sample collection, or you may be asked by the study doctor or staff to stay at the clinic until the 24 hour blood sample is collected.

At delivery (where possible):

If it is possible, both your blood and blood from the umbilical cord will be taken just after the delivery of your baby by the study staff. About one teaspoon will be taken.

4 – 8 weeks after you have given birth:

We would like to perform the PK sampling procedure again, between 4 and 8 weeks after you have given birth and take blood from you at the 6 timepoints.

Blood will be drawn 6 times over 24 hours. These time points are: before you take your dose of TB medication (pre-dose) and then 2, 4, 6, 8, and 24 hours after you have taken your dose of bedaquiline, clofazimine and levofloxacin (post-dose).

During this visit and if you are breastfeeding your baby:

- We would also like to take breastmilk samples from you at 5 timepoints: pre-dose and at 2, 4, 6, and 8 hours post-dose. We will ask you to express 20ml of breast milk into a sterile container for us.
- A blood sample (about 2 ml or half a teaspoon) will also be taken from your breastfed baby/ies at a random timepoint (once per baby) over the 8 hour PK visit. This is to help us see how much of the TB medicines are found in the baby's blood. This will either be taken by the study staff in a tube or we will prick your baby's heel.

If available, the following additional samples will be taken from your baby:

If you are breastfeeding your baby, we would like to take a blood sample (2ml or half a teaspoon) from your baby, either by the study staff in a tube or we will prick your baby's heel. This would happen at two study visits, when:

- You are close to finishing your treatment.
- And 1-3 months after you have finished your treatment.

Please note that these procedures are in addition to the regularly scheduled procedures that will take place for the main study.

5. Reimbursement for sub-study participation

You will not be paid to participate in this sub-study but the additional time, inconvenience and expenses that you may incur, will be reimbursed adequately, according to SAHPRA requirements. You will therefore be reimbursed R300, for the intensive PK study visits. This will be in addition to the compensation you receive for your regular visit.

6. Participant questions

Did the participant raise any questions? **Please circle one:**

YES / NO

If YES, what were they:

PARTICIPANT INFORMED CONSENT SIGNATURE PAGE FOR PARTICIPANTS (>18 YEARS) WHO ARE PREGNANT

I declare that:

	Participant Initial and date
I have received, read and understood the above written information (INFORMATION LEAFLET AND INFORMED CONSENT FOR PARTICIPANTS WHO ARE PREGNANT (>18 YEARS)) as part of the BEAT Tuberculosis (Building Evidence for Advancing new Treatment) trial.	
I am aware of the potential risks to myself and my baby.	
I have had sufficient opportunity to ask questions and (of my own free will) declare myself content to continue to participate in the BEAT Tuberculosis study, given that I am currently pregnant.	

PARTICIPANT:

Printed Name	Signature / Mark or Thumbprint	Date and Time
--------------	--------------------------------	---------------

PERSON OBTAINING INFORMED CONSENT :

DESIGNATION (if other than the study doctor): _____

I herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study

Printed Name	Signature	Date and Time
--------------	-----------	---------------

STUDY DOCTOR:

Printed Name	Signature	Date and Time
--------------	-----------	---------------

TRANSLATOR (if applicable):

Printed Name	Signature	Date and Time
--------------	-----------	---------------

WITNESS (if applicable):

Printed Name	Signature	Date and Time
--------------	-----------	---------------

OPTIONAL INFORMED CONSENT: PREGNANCY PK SUB-STUDY

I have been informed by the study staff about the nature, purpose and details of the Pregnancy PK sub-study. I also understand that if I agree to take part in the sub-study I may, at any stage, without prejudice, withdraw my consent and participation in the sub-study. **Tick one:**

☐ **YES**

☐ **NO**

I consent to take part in the additional Pregnancy PK Sub-study. **Tick one:**

☐ **YES**

☐ **NO**

PARTICIPANT:

Printed Name	Signature / Mark or Thumbprint	Date and Time
--------------	--------------------------------	---------------

PERSON OBTAINING INFORMED CONSENT :

DESIGNATION (if other than the study doctor): _____

I herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study

Printed Name	Signature	Date and Time
--------------	-----------	---------------

STUDY DOCTOR:

Printed Name	Signature	Date and Time
--------------	-----------	---------------

TRANSLATOR (if applicable):

Printed Name	Signature	Date and Time
--------------	-----------	---------------

WITNESS (if applicable):

Printed Name	Signature	Date and Time
--------------	-----------	---------------