INSIGHT PATIENT INFORMED CONSENT

STUDY INFORMED CONSENT FORM

TITLE: A phase 2b study to evaluate the efficacy, safety and pharmacokinetics of a combination of Bictegravir, Emtricitabine, and Tenofovir Alafenamide Fumarate for treatment of HIV-1 infection in patients with drug-susceptible tuberculosis on a Rifampicin-based treatment regimen

INFORMATION FOR PARTICIPANTS

Short Title: INSTI's FOR THE MANAGEMENT OF HIV-ASSOCIATED TB **(**INSIGHT)

Principal Investigator:	Dr Anushka Naidoo
Address:	719 Umbilo Road Doris Duke Medical Research Institute (2nd floor) Nelson R Mandela School of Medicine University of Kwa-Zulu Natal Durban, 4013
Telephone:	031 655 0500
Regulatory Authority:	South African Health Products Regulatory Authority (SAPHRA)
Ethics Committee:	University of KwaZulu Natal Biomedical Research Ethics Committee (UKZN BREC)

Information Sheet and Consent to Participate in Research

Instructions:

1. Please read and understand the information given below
2. If you have any questions or need any explanations, then please feel to discuss with the person handing you the Informed Consent Form at any time.
3. Once you have agreed to participate in the study and you will be asked to sign the Informed Consent form. We will give a copy (if you wish to have one) and a copy will be placed in your file. The original will be kept in a secure room by the study coordinator

Date: _____

Dear Sir/Mam,

My name is …… from the Centre for AIDS Programme in South Africa (CAPRISA). We are performing a research study in Durban, Kwa-Zulu Natal. The Principal Investigator for this study is Doctor Anushka Naidoo, who is a researcher and is part of the CAPRISA TB HIV Treatment Research Programme. Her telephone number is 031 655 0553 and email is: anushka.naidoo@caprisa.org

Research Summary (Key Information)

The information in this section is intended to be an introduction to the study only. Complete details of the study are listed in the sections below. If you consider participating in this study, the entire document will be discussed with you before you make your final decision. You can ask questions about the study now and at any time in the future.

We are searching for better ways and new options to treat HIV for those that also have TB. The purpose of this study is to check whether a fixed-dose single tablet ART regimen including Bictegravir, Emtricitabine and Tenofovir Alafenamide (Biktarvy) is safe and can lead to similar viral suppression to current standard of care ART drugs used for treatment of HIV in South Africa [Dolutegravir, Tenofovir and Lamivudine (TLD)]. We are enrolling participants who 18 years and older, have been newly diagnosed with HIV and never been on any ART treatment previously or had prior exposure to ART medication. You also, have to have TB at the time of starting this study and must be initiating on or taking rifampicin-based treatment for your TB. We are planning to follow participants up for 48 weeks. During screening, enrolment and follow-up visits, the medical study staff will do medical examinations on you and take bloods for safety monitoring. This will allow the medical staff to monitor the effects of the ART drugs on your HIV infection and to make sure that you receive the best care.

You may feel discomfort when a blood sample is taken. Side effects of both TB and HIV treatment can occur. The combinations of treatment and twice daily dosing of HIV treatment during TB treatment can mean that you may get more side effects.

You may be provided with an Electronic Monitoring device or a pillbox to measure your adherence to your ART and/or TB medication.

Your participation in this study will not cost you extra charges. If you do decide not to participate, your medical treatment will not be affected in any way.

1. Invitation to participate in the study

You are being invited to take part in a research study. Research is a way of finding the answer to a question. Before you decide to participate, it is important that you 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 others if you wish. Your participation is voluntary which means you can choose whether or not to participate. Please take time to consider the following information before deciding whether you wish to participate in this study. We will explain this carefully but please feel free to ask questions.

We have approached you to take part in this study because of your recent diagnosis of HIV as well as currently having Tuberculosis (TB).

2. Why is this being done?

HIV is treated with many types of antiretroviral therapies (ART) that are available at all Department of Health (DoH) facilities. Being infected with both TB and HIV, leads to challenges especially with ensuring the best treatment options and outcomes. For this reason, we are searching for better ways and new options to treat HIV for those that also have TB. The purpose of this study is to check whether a fixed-dose single tablet ART regimen including Bictegravir, Emtricitabine and Tenofovir Alafenamide (Biktarvy) is safe and can lead to similar viral suppression to current standard of care ART drugs used for treatment of HIV in South Africa. This combination drug will be known as ***Biktarvy*** in this study. We will compare this new type of combination to another ART regimen which is Dolutegravir, Tenofovir and Lamivudine (TLD). TLD is standard of care treatment that you will get when you go to the clinic if you are HIV positive. ***Biktarvy*** is not available in South Africa currently, and if this treatment is successful, it may become an option for treatment and care of HIV patients.

Standard Combination: Dolutegravir, Tenofovir and Lamivudine (**TLD**)

New Combination: Bictegravir, Emtricitabine and Tenofovir Alafenamide (***Biktarvy***).

3. Who can take part in this study?

If you are 18 years and older, have been newly diagnosed with HIV and never been on any ART treatment previously or if have had ART treatment before then you qualify for the study. You also, have to have TB at the time of starting this study and must be initiating on or taking rifampicin-based treatment for your TB (for not more than 8 weeks) to be able to qualify for the study.

4. Is it necessary for me to take part in the study?

The decision to take part in the study is up to you. It is a voluntary decision. You do not have to give a reason if you don't want to be in it. After reading this information and agreeing with what you have read - if you decide to take part in the study - you will be asked to sign an Informed Consent form. If you decide not to take part, there will be no loss of benefit and you will receive standard HIV treatment and continue to receive your TB treatment as part of standard care. If you decide to take part in the study, but change your mind later, you will be free to withdraw from the study at any time. If you choose to withdraw from the study, your medical care will not be affected if you do not want to take part anymore.

5. What does the study involve?

We will explain the study to you in 3 parts which are as follows:

Part 1: Screening Phase

Part 2: Enrolment/Randomization Phase

Part 3: Treatment Phase/Follow-up Phase

Part 1: Screening Phase

The first part is called “screening phase” we will need to verify your age by checking your South African Identity Number or any other official document. We will also perform tests to check whether you are suitable to participate in the study. These tests will include doing an HIV test to confirm your HIV status, taking your medical history (your health in the past) and performing a medical examination. We may also ask for a sputum to verify your TB status and to test if you are resistant to any of the TB drugs that you are currently taking. We would also like to know when you began TB treatment so that we can make sure you meet all the screening criteria. Blood tests will be also performed to make sure that there are no abnormalities (problems) that would prevent you from taking part in the study or cause harm to you. We will also conduct HIV related blood tests in order to check your CD4 cell count and viral load before you start treatment. It is therefore important for study staff to know your HIV status, so that you can be treated accordingly. The HIV test will be performed with pre- and post-test counselling (a study counsellor or nurse will discuss this with you to guide you about HIV-AIDS and related test procedures).

We will also review all other medications that you may be taking to make sure that these medications do not cause further harm to you when you start your ART treatment. The blood tests at this stage will require approximately 5 teaspoons of blood. If you are a woman/female of childbearing age then a urine pregnancy test will be conducted to ensure that you are not pregnant, and you will need to be on hormonal contraception during the study to prevent pregnancy for the duration of the study. If you are HIV negative, do not have TB, have resistant TB, are pregnant or have been taking rifampicin for more than 8 weeks then you will not be able to be enrolled in the study as you do not meet the criteria.

Part 2 and 3: Enrolment Phase/Follow-up Phase

At this stage – all patients participating in this study will be divided into 2 arms in a 2:1 ratio. That means, 80 people will be enrolled into the New ART Treatment Arm and 40 people will be enrolled into the Standard ART treatment Arm. Each arm will have a different type of ART treatment. One of these arms is the New ART treatment combination (BIC) and the other is the Standard ART Treatment (TLD). The results of the study shall be compared to see if one treatment is better than the other. The best way of fairly dividing people into arms is to use what is called "random allocation". So, you will either get treatment from the BIC Arm or the DTG Arm and neither the patient nor the health care staff can choose the treatment. At the study entry visit, you will be assigned to one of these two treatment arms:

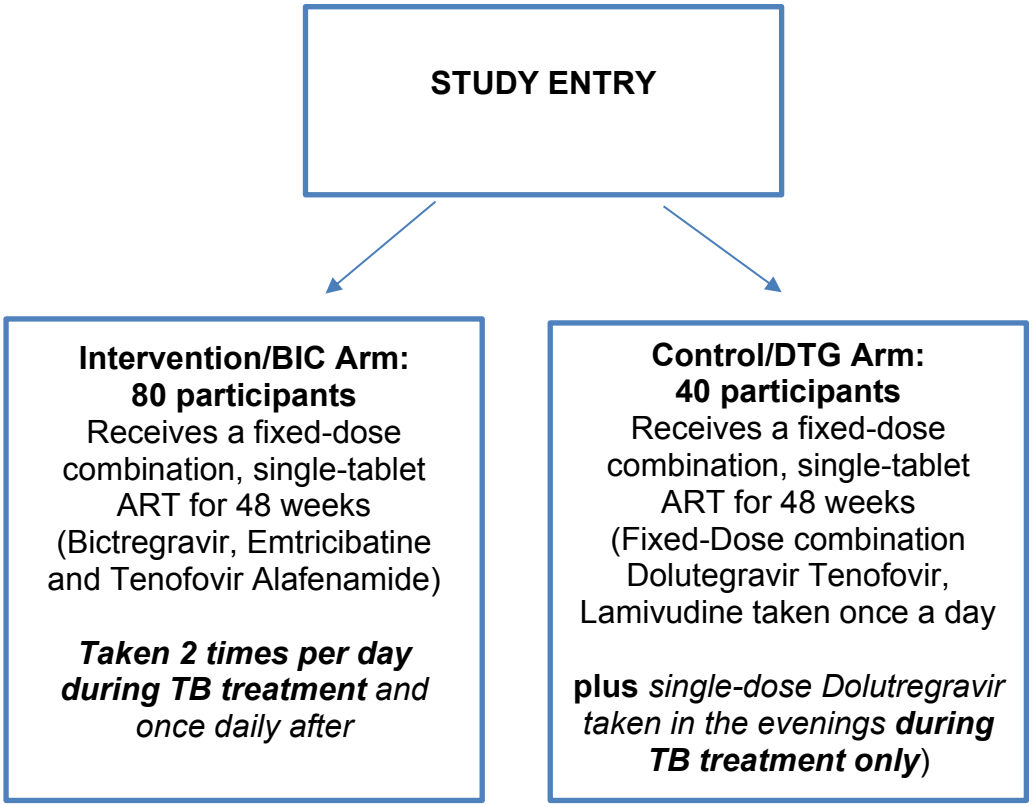

Figure 1: Patient Allocation to Study Groups

If you are placed into Intervention Arm you will be expected to take a fixed-dose single tablet combination of 3 drugs twice a day during TB treatment (and 2 weeks after rifampicin stopped) then once daily after over the duration of the study (or 48 weeks) thereafter you will move to the current standard of care HIV treatment.

If you have been placed into Control Arm, you will be required to take a fixed-dose single tablet combination of 3 drugs (Dolutegravir, Tenofovir, Lamivudine taken once a day) *plus* Dolutegravir single tablet in the evening during TB treatment (and 2 weeks after rifampicin stopped) only. After the study, you will continue on the same ART or appropriate SOC treatment.

All safety and other test results will be checked by the study doctors during the study including your HIV Viral Load blood results and CD4 cell counts.

CAPRISA will provide the ART treatment in the intervention/BIC and Control/DTG arm to you during the study.

During enrolment and follow-up visits, the medical study staff will continue to do medical examinations on you and take bloods for safety monitoring. This will allow the medical staff to monitor the effects of the ART drugs on your HIV infection and to make sure that you receive the best care. You will also be requested have bloods taken for storage and later testing that will be used to check if you are resistant to any of the ART that was administered to you and will be stored if you agree/consent to blood or other sample storage. Hair samples which are optional at follow up may also be taken if you consent as we would like to further look at ART drug levels in hair and how ***Biktarvy*** interacts with other drugs. You are required to take all your medication as prescribed by the study doctor and make sure that you continue to collect your ART treatment for the full 48 weeks. Medical staff will also closely monitor whether you are resistant to any of the ART drugs as well as the side-effects that you are experiencing. Additional blood may be collected for tests that are not part of the study but are part of routine care or if the doctor feels this is necessary for your medical care. Pregnancy tests will also be done throughout enrolment and follow-up phase. You will not be required to be hospitalised during any points of the study. If you unable to travel to the clinic during any of the follow-up visits, we request your permission to be contacted by phone by the study staff to check how you are doing and if you have any concerns.

6. How many people will take part in the study?

A total of approximately 120 participants are expected to participate in the study with 80 in the Intervention/BIC arm and 40 in the Control/DTG arm.

7. Use of stored samples

Samples will be collected and stored in order to test for resistance to any of the ART drugs and other testing including determining drug levels in your blood and if genetic variability in enzymes that break down ART or TB drugs change drug levels in your blood. About 4 teaspoon of blood will be required for this. We may also use stored samples/specimens for future testing. The research team may use these samples to confirm test results or to do an additional new test if required. Your samples will not be sold or used in other products that make money for researchers. Should you decide not to have your samples stored this will not affect your ability to take part in the study. Your decision will not affect the quality of care you receive at the clinic

To protect your identity your sample container will not have your name or any information that may identify you. Only your patient number will be used on sample containers. If you do not agree, then samples for storage will not be collected. If you agree now and later change your mind, your sample will not be used for future testing. No matter what you decide, it will not affect your participation in the study and this will not affect the quality of care you receive from study staff.

The stored samples may be used for future research, to confirm test results, or to do additional testing. Your samples will not be sold or used in products that make money for the researchers. Any studies that use your samples will be reviewed by the Biomedical Research Ethics Committee of the University of KwaZulu Natal.

The researchers do not plan to contact you or your regular doctor with any results that are done on the stored samples after the study has been completed. This is because research tests are often done with experimental procedures so the results from one study are generally not useful for making decisions on managing your health. Should a rare situation come up where the researchers decide that a specific test result would provide important information for your health, the researchers will notify the study doctor who will try to contact you or your regular doctor. If you wish to be notified of this type of test result, you need to make sure that you contact the study nurse or doctor with any changes to your phone number or address. If you want your regular doctor to be told about this kind of test result, you need to provide the study team with the contact details of your regular doctor.

_____ YES, I agree to have my samples stored

_____ NO, I do not agree to my samples being stored

8. Pharmacokinetic Study

The INSIGHT study also includes a pharmacokinetic (PK) study **which is part of the main study**.

The purpose of collecting PK samples in the study is to measure the amount of the ART drugs or TB drugs in your blood when taken twice a day. This will add valuable information to the INSIGHT study. Before you agree to take part in the INSIGHT study or not it is important to understand the procedure, risks, benefits and discomforts. You will be requested to undergo additional blood tests at these PK study visits and as outlined in the study protocol.

These are the procedures that will be followed for all participants if you decide to take part in the INSIGHT study:

If you are selected to be part of the BIC arm

- While taking rifampicin, you will be required to provide a blood sample within the study clinic just before your morning dose and 1 to 4 hours after you haven a dose at the clinic at **Day 28 (Visit 3) and week 12 (Visit 5)**
- After you have completed your TB treatment, you will provide a blood sample within the study clinic just before your morning dose and 1 to 4 hours once you have taken the dose at the clinic at **week 32 (Visit 7)**

If you are in the BIC or DTG arm

- you will be required to provide a blood sample within the study clinic just before your morning dose at **week 8, 24 and 48 (Visit 4, 6 and 9)**

The blood tests for the pharmacokinetic study will require 1-2 teaspoons of blood

The study team will arrange a time for the blood sampling. On the appointed day you need to arrive at the study clinic early in the morning.

It is important ***NOT*** to take any ART treatment before your arrival at the study clinic (on the day of the PK visit). You will be given your morning dose of ART treatment for the day of the PK visit at the study clinic. You will also be asked to record the time of your last dose of ART or TB treatment taken at home.

We are also undertaking a Pharmacokinetic sub-study in a smaller number of patients who agree to this study and are allocated to the BIC arm. This Pharmacokinetic sub-study **called a semi-intensive study** will collect blood samples at more timepoints on PK sampling days. Your decision to participate in this additional sub-study, or not, will not affect your participation in the INSIGHT study. Before you agree to take part in the study or not it is important to understand the procedure, risks, benefits and discomforts.

- While taking rifampicin, you will be required to provide a blood sample within the study clinic just before your morning dose of ART and at 1, 2, 4, 6 hours after the morning dose in the clinic and again after 8-12 hours at **Day 28 (Visit 3) and week 12 (Visit 5)**

- After you have completed your TB treatment, you will provide a blood sample within the study clinic just before your morning dose and at 1, 2, 4, 6-8 hours after the morning dose in the clinic and again after 24-25 hours (i.e the next day morning) when you will return to the clinic to have a sample taken before your morning dose of ART at **week 32 (Visit 7)**

The blood tests for the semi-intensive pharmacokinetic sub-study will require 5-6 teaspoons of blood

The study team will arrange a time for the blood sampling. On the appointed day you need to arrive at the study clinic early in the morning.

It is important ***NOT*** to take any ART treatment before your arrival at the study clinic (on the day of the PK visit). You will be given your morning dose of ART treatment for the day of the PK visit at the study clinic. You will also be asked to record the time of your last dose of ART or TB treatment taken at home.

Please indicate your participation in the **semi-intensive sub-study** should you be allocated to the BIC arm:

_____ YES, I agree to take part in the semi-intensive pharmacokinetic sub-study

_____ NO, I do not agree to take part in the semi-intensive pharmacokinetic sub-study

9. What are some of the situations where my participation in the study may be terminated?

A. We may stop your participation in the study under the following conditions:

- Your doctor is of the opinion that your ART treatment is going to fail (Treatment failure)
- If you require another ART treatment as you are resistant to the treatment on the BIC arm
- If you have poor kidney or liver function after we have received your blood results before you have taken any ART treatment

- Review of your health suggests that further participation in the study may cause you more harm than benefit
- You are missing a number of clinic visits and repeatedly do not follow study instructions and not taking study drug as per the directions and this may result in more harm than benefit
- The study is cancelled by the South African Health Products Regulatory Authority (SAHPRA), or the University of KwaZulu Natal Biomedical Research Ethics Committee.
- A Safety Monitoring Committee (SMC) recommends that the study be stopped early. The SMC is a group of experts who are not involved in the study, but who monitor it and look after the safety of patients. This group meets during the study follow up and makes recommendations for the study.

B. The study may be suspended in following cases:
   - Reports of severe and significant side effects
   - Reports suggest that the new regimen under trial is not effective in treating HIV.

If any of the above happens then your HIV and TB and any other health condition will be treated as per standard care.

10. What other choices do I have besides this study?

If you choose not to enter the study then you may access ART treatment from the local government clinic. The care that people on the DTG arm is similar to the care that you will receive if you did not participate in the study. Certain TB drugs and HIV drugs, laboratory tests to monitor how well these drugs are working, and quality medical care may or may not be available to you outside the study. The clinic staff will discuss with you other treatment choices in your area and the risks and the benefits of all the choices.

11. What about Confidentiality including the POPI Act?

Data information referred to herein, includes research and clinical practice records, medical records and personal information (such as your name, address, contact details, date of birth, age, gender, occupation, medical scheme membership and health information) that is collected during the course of the study.

Under the data protection law and in accordance with the provisions of the Protection of Personal Information Act No. 4 of 2013, CAPRISA will only process your data to provide you with the clinical research, trial and treatment that we agreed to provide to you and to comply with all of our legal and regulatory requirements.

The study research team will give you a unique number once you are enrolled into the study. A different number will be given for each participant in the study. This unique number and not your name (or any other information that could be used to identify you) will be used for all of your study-related records to maintain confidentiality. Your data will be held physically or electronically and it will be retained by CAPRISA for such periods as may be prescribed by or permitted in terms of the law and for lawful purposes, including for historical, statistical and research purposes. CAPRISA will inform you if any person has unlawfully obtained access to your data. Your medical records and the list of names, addresses and code numbers will be kept in a locked room. Only the study staff will have access to these records. CAPRISA has implemented measures to ensure that your data will be kept confidential and protected against destruction and unauthorised access. Where your data is hosted on servers managed by third-party service providers, CAPRISA will ensure that such third-

party service providers maintain the same data protection policies and procedures and that your data is stored in a manner that is compliant with the law. Any publications of this study will not use your name. The site will attempt to keep your personal information confidential. However, we cannot promise complete confidentiality asyour personal information may be disclosed if required by law. Your details may be seen by the site's ethics committee, Human Research Protection, study monitors, and drug companies that support this study. Your records for the study may be reviewed by the University or other governmental regulatory authorities and study monitors to assure the accuracy and quality of the records and the correct conduct of the research study. This study is protected by a Certificate of Confidentiality that helps keep your information private when stored in the U.S.

12. What are the risks and discomforts associated with this study?

These are a list of risks that may arise:

- Until this study is completed, there is no way of knowing for sure if Biktarvy is fully effective in treating HIV in those patients with TB treatment on rifampicin, however your treatment progress and safety results will be carefully monitored throughout the study to ensure that your treatment is working well.
- The fixed dose taken twice daily may have some side effects. Some of the side-effects are in attachment B. Studies have shown that it is safe with no increase in toxicity. Some common side effects of the drugs in both the intervention and the control/standard of care arm may include nausea, diarrhoea and headache. If you have any questions concerning the study drugs, standard of care ART or any additional drugs you may be put onto during your course on this study, you can ask any of the clinical staff at the CAPRISA site or contact the study investigators on the contact details below.
- During certain study visits, the staff nurse will draw blood from you. Taking blood may cause some discomfort, bruising or bleeding at the site where the needle enters your body. You also may feel lightheaded and in a rare case faint. Although unlikely, the area also may become infected.

13. What happens if I become pregnant?

If you are pregnant or breastfeeding you will not be allowed to take part in this study because the effects of the study drugs on a baby still in the womb and babies being breast fed, is unknown. If you are women able to fall pregnant and you are having sex, you must use two reliable methods of birth control whilst on the study. This will be discussed with you by the study staff. The methods of contraception (birth control) include:

- Male or female condom with or without a spermicidal agent (cream or gel that kills sperms)
- Diaphragm or cervical cap with a spermicide
- IUD (Intrauterine device) or hormone-based contraception.

If you think you may be pregnant at any time during the study, please tell the study staff right away. If you become pregnant while on study, the study staff would like to obtain information from you

about the outcome of the pregnancy (even if it is after your participation in the study). The study staff will talk to you about all your choices.

14. What are benefits associated with the study?

If you decide to take part in this study, there may be a direct benefit to you, but no guarantee can be made. Medical staff at the CAPRISA site will follow your health more closely which may help you feel better. Being a newly diagnosed with HIV, you will also be closely monitored and managed by study staff. This means that medical examinations and bloods for safety monitoring are done more frequently than done as part of standard care outside the study. All treatment and medical care and advice in the study is available free of charge as you would receive as part of standard of care.

15. Will I receive payment?

Participants enrolled into this study will be reimbursed R250 for every study required scheduled visit. For all the PK study visits, you will be given R350. See **Attachment A** for required study visits. For pre-specified staff initiated split, interim and unscheduled visits, you will be reimbursed R150.

16. What are the costs to me?

There will be no cost to you for the study related visits, physical examinations, laboratory tests or other procedures.

17. What happens if I am injured or have concerns?

Based on what we know now, it is unlikely that you will be injured as a result of being in this study. If you are injured as a result of being in this study, you will be given immediate necessary treatment for your injuries at the CAPRISA Clinical Research Site. You will not have to pay for this treatment. You will be told where you may receive additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries. You do not give up any legal rights by signing this consent form. If you have any concerns about any aspect of this study, you should ask to speak to the study staff who will be able to better answer your questions.

All study staff will be indemnified and will also be regulated by South African Health Products Regulatory Authority and the University of KwaZulu Natal Biomedical Research. The CAPRISA Clinic has taken out an insurance policy for this study. Should you acquire an injury that is as a result of the study, please inform the study staff immediately or contact the persons listed at the end of this form. A CAPRISA staff member will assist you with any valid insurance claims.

This research study is covered by an insurance policy (Policy number: 4000/24885; Insurer: Highgrove Financial Services (Pty) Ltd) taken out by CAPRISA, 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, 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.

18. What are my rights as a volunteer in a research study?

You can decide whether or not you wish to take part in this study. If you choose not to take part in the study, the care you would normally receive will not be affected. You can also leave the study if you feel comfortable doing so. The site staff will tell you about any new information from this study (or other studies using similar drugs) that may affect your health, welfare, or willingness to study in this study. Any stored samples that can still be identified as yours will be destroyed if you wish (please speak to study doctor)

19. What will happen to the results of the research study?

The results of this study will be used by researchers, doctors and policy makers to determine what is the best way to treat HIV. If the single-tablet fixed-dose combination of Biktarvy proves effective the results may be used by to make this drug available to patients in South Africa and may inform national guidelines. The results will be published in medical journals and presented at conferences but you will not be identified in any reports or publications. CAPRISA will destroy your data in a manner that is compliant with the law, as soon as your data is no longer required. You can request access to your data at any time and you can request CAPRISA to update or correct your data, in the event that it is outdated. You can also withdraw your consent for the processing of your data at any time, in which event CAPRISA reserves its right to terminate its relationship with you.

Should you have any concern about the processing of your data by CAPRISA, you can raise this with any of the research and/or treatment practitioners.

20. What will happen to any samples I give?

If you consent to storage of samples, we may take some extra blood that will be stored under the supervision (custodianship) of Dr Anushka Naidoo. This will include up to 1 teaspoon of blood which we will use for ART resistant testing and approximately 10-12 teaspoons of blood for other tests outlined above. We will collect these samples during procedures that have been described already before you receive the study medication. We will take these samples at timepoints outlined in Attachment A. We will also take bloods in order to make sure you have not developed side effects to the study treatment. Stored samples may also be analysed to better understand the way different ART drugs in the intervention arm affect each other and the HIV infection. In line with international guidelines, samples will be stored for approximately ten years after study completion and closeout. Samples may be analysed outside of this country if it is not possible to do the analysis in South Africa. Any samples will have only an identification number and the results will be anonymous. There will be no way that you or your personal details can be identified from these samples. Any study

using your stored samples will need to be approved by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal. You may decide to participate in this study but not to allow storage and future use of your samples.

21. Who has approved the study in South Africa?

The Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC reference number:(BREC/00001300/2020), The Provincial Department of Health of KwaZulu-Natal and the The South African Health Products Regulatory Authority.

22. Contacts and Questions

You may ask any questions you have now or contact the below individuals later. If you have any urgent health concerns or, you are encouraged to contact:

Dr Anushka Naidoo (Principal Investigator), telephone number: 031 6550553/ 082 928 3244, email: anushka.naidoo@caprisa.org

In case of any questions regarding the Welfare and rights of participants, you should contact:
BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

If you have any questions regarding the study that was not answered to your satisfaction by your doctor and the Ethics Committee, you should write to The South African Health Products Regulatory Authority (SAHPRA) at:

The Chief Executive Officer
South African Health Products Regulatory Authority
Loftus Park
Building A
402 Kirkness Street
Arcadia, Pretoria
0083

E-mail: Boitumelo.Semete@sahpra.org.za
Tel: 012 501 0413

You will be given a copy of the information sheet and a signed consent form to keep if you wish to do so.

Thank you for taking the time to read this information sheet.

	Initial or Thumbprint
I have read or had the participant information sheet (version_____) about enrollment into the INSIGHT study read to me in full. I have had opportunity to consider the information and to ask questions and have had my questions answered completely.	
I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
I understand that any relevant sections of my medical notes and data collected during the study may be looked at by responsible individuals from the Sponsor or from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
I agree to take part in the above study and will comply with the study medication and follow-up as explained in the patient information sheet.	

PLEASE INDICATE YES OR NO TO THE FOLLOWING QUESTIONS AND PUT YOUR INITIALS IN THE LAST COLUMN			**Please initial box**
I agree to be contacted by telephone for follow-up appointments.	YES	NO	
I agree for samples taken from me to be retained, stored and used in future approved research projects.	YES	NO	
I agree to be contacted via SMS	YES	NO	
I agree to off-site visits by study personnel. During these off-site visits study procedures may be conducted.	YES	NO	

Name of Participant	Signature / Thumbprint (with witness)	Date
Name of Person taking consent	Signature	Date

The participant is unable to sign and thumbprint used. As a witness, I confirm that all the information about the study was given and the participant consented to taking part.

Name of Impartial Witness *(if participant thumbprint used)*	Signature	Date

Relationship of Impartial Witness to participant (*if no relation, write "no relation" and provide explanation who you are, e.g. caretaker of another patient*)

Attachment A: Schedule of Events

INSIGHT Schedule of Evaluations:									
Description	**Screening**	**Randomization and Enrolment***	**Follow-up**						**End of study**
Trial Visit	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**
Day/week	**Screening**	**D0 Enrolment**	**D28/ Week 4**	**Week 8**	**Week 12**	**Week 24**	**Week 32**	**Week 40**	**Week 48**
Informed consent	X								
Age verification	X								
HIV confirmatory test	X								
Urine pregnancy test in females	X	X	X	X	X	X	X	X	X
Vital signs (incl. height and weight)	X	X	X	X	X	X	X	X	X
Targeted Physical exam/Clinical safety monitoring	X	X	X	X	X	X	X	X	X
Verification of eligibility		X							
Randomization		X							
Safety bloods (Hb, Urea, Creatinine, e-GFR, ALT, AST, Bilirubin, Amylase, platelets FBC *and other* ***as clinically indicated***) #	X	**X**[#]	X	X	X	X	X	X	X
HEP B surface antigen	X			X		X			X
Drug-susceptible TB diagnosis/confirmation of previous results (GeneXpert (including Rif resistance))	X								
Sputum Smear testing*	X			X		X			
Sputum Culture* (genotypic/ phenotypic testing for RIF/INH resistance at month 6 only if positive)				X		X			
CD4+ cell count	X					X			X
HIV-RNA viral load **	X		X	X	X	X		X	X
ART administration		X	X	X	X	X	X	X	X
TB treatment (duration may vary)	X	X	X	X	X				
AEs/SAEs assessment			X	X	X	X	X	X	X
TB associated IRIS assessment			X	X	X				
Concomitant medication review	X	X	X	X	X	X	X	X	X
PK blood draws***			X	X	X	X	X		X
Dry blood spots for PK analysis***			X	X	X	X	X		X
Pharmacogenetic sample storage (buffy coat)		X							
PBMC Cell Storage		X				X			X
Hair sample##			X	X	X	X	X		
Stored plasma sample for HIV-1 genotyping$		X				X[$]			X[$]
Electronic Dose Monitoring ®		X	X	X	X	X	X	X	X

Attachment B: Study Drug Side Effects

Drug	Common Side – Effects
Biktarvy	-Diarrhea, nausea, and headache -Changes in your immune system (Immune Reconstitution Syndrome) can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having any new symptoms after starting your HIV-1 medicine. -New or worse kidney problems, including kidney failure. Your healthcare provider should do blood and urine tests to check your kidneys when starting and during treatment with BIKTARVY. Your healthcare provider may tell you to stop taking BIKTARVY if you develop new or worse kidney problems. -Too much lactic acid in your blood (lactic acidosis). Too much lactic acid is a serious but rare medical emergency that can lead to death. Tell your healthcare provider right away if you get these symptoms: weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat. -Severe liver problems. In rare cases, severe liver problems can happen that can lead to death. Tell your healthcare provider right away if you get these symptoms: skin or the white part of your eyes turns yellow, dark “tea-colored” urine, light-colored stools, loss of appetite for several days or longer, nausea, or stomach-area pain.