Document:
Informed Consent Form

Official Study Title:
SEARCH CAB LA Dynamic Choice HIV Prevention Study Extension
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INFECTIOUS DISEASES RESEARCH COLLABORATION

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Extension of SEARCH SAPPHIRE Dynamic Choice Prevention Study

Extension of SEARCH SAPPHIRE Dynamic Choice Prevention Study – Informed Consent Form

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This is a clinical research study. The Principal Investigator, who is the person in charge of this study, or one of the other members of the study team from the Extension study will explain the study to you.

STUDY SUMMARY

The objective of the DCP Long-Acting Cabotegravir (CAB-LA) Extension study is to reduce HIV incidence and to improve community health with multi-sector, scalable interventions. This Extension will examine if enhanced HIV prevention options, including CAB-LA, is superior to the current standard of care.

CAB-LA is an injectable HIV-prevention method, taken in clinic every 4 weeks for two times, and then every 8 weeks thereafter. CAB-LA is very effective to prevent HIV if taken accordingly.

Introduction: We are asking you to consider taking part in a research study being done by researchers from Makerere University (MU), the Infectious Diseases Research Collaboration (IDRC), the University of California, Berkeley (UCB), and the University of California, San Francisco (UCSF). The U.S. National Institutes of Health (NIH) pays for this study.

The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends and health care team.

Purpose of the study:

The researchers want to study ways to improve HIV prevention programs in your community. This study will compare the effects, good and/or bad, of enhanced dynamic choice prevention choices, including CAB-LA, versus standard of care to find out which is better. In this study, you will either continue receiving the enhanced dynamic choice options, with the addition of CAB-LA, or standard of care. You will not get both.

Study Procedures:

If you choose to continue in this study, you will remain assigned to the randomization arm, either intervention or control, you are currently in. If you are in the intervention arm, we will offer you the choice of CAB-LA as one of your DCP selections; if you are in the control arm, you will remain being treated per MoH standard-of-care guidelines. Regardless of which group you are in, (Pre-Exposure Prophylaxis) PrEP and (post-exposure prophylaxis) PEP medications will be available to you according to standard practices in the community. PrEP is a daily pill you can take to prevent HIV (year-round) and PEP is a daily pill you can take after an HIV-exposure for a 28-day course. This extension will cover the time period between after the current 48 week study ends and 48 weeks beyond when the intervention arm has access to CAB-LA.

Possible Risks and/or discomforts: There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

- Breach of confidentiality
- Sensitive Discussions
- Pain or discomfort from Hair Sample or Blood Collection (when applicable)

There are rare but serious risks of participation if you are in the intervention arm and decide to take CAB-LA, like:

- Pain, tenderness, hardened mass or lump, swelling, bruising, redness, itching, warmth, abscess, discoloration, or loss of sensation at the injection site
- Stomach pain
- Vomiting

We'll tell you about the other risks later in this consent form.

Possible Benefits:

There will be no direct benefit to you from participating in this study. The enhanced measures to improve PrEP and PEP delivery, if you are assigned to the group that receives it, may help you stay on medications, receive care, or reduce the likelihood of acquiring HIV infection, but this cannot be guaranteed. Your participation in the study may benefit the community, scientists and doctors who work on providing HIV care in health centers such as yours.

Your other options:

You do not have to participate in this study. Your other choices may include:

- You can be put on to the national standard of care for HIV prevention. Your access to PrEP and PEP through the clinic will not be affected if you decide to stop participating in the study.

Please talk to your doctor about your choices before agreeing to participate in this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.

Why is this study being done?

Providing successful HIV prevention methods can be difficult for doctors, nurses, hospitals and local governments. When you first consented to this study, there were two ways HIV could be prevented: by taking PrEP or PEP. PrEP is a prevention method that involves HIV negative people taking antiviral drugs to try to prevent infection for as long as they are at risk. PEP medications are taken immediately after a suspected exposure to HIV through sexual contact or other ways, and is normally taken for a month. Now, there are three ways to prevent HIV: PrEP, PEP, and Long-acting Cabotegravir (CAB-LA), which is an injectable prevention method, taken in clinic every 4 weeks for two times, and then every 8 weeks thereafter. CAB-LA is approved for use for HIV prevention in the United States for adolescents 12 years and older and weighing at least 35 kilograms. CAB-LA is not approved for HIV prevention in Kenya and Uganda but is under review. You will be able to take this drug on an investigational basis in this clinical trial. This extension study will continue delivering these options as before, that seek to improve existing PrEP and PEP services, with the new addition of CAB-LA. This study will continue to include convenient access to clinicians for changes to your HIV prevention methods, the offer of other health services to make visits more efficient, options for PrEP and PEP delivery (if not on Long-Acting CAB-LA), and discussions with the clinician on ways to overcome any barriers to receiving these services.

What is the usual care for my condition? The usual care for HIV prevention is standard of care per country MoH guidelines

How many people will take part in this study?

Approximately 600 participants will take part in this study

What will happen if I take part in this study?

Before you begin the main part of the study…

You will need to re-enroll, as described below.

Enrollment in the Extension

Enrollment will take place at a health facility or in a community location. Study staff will review your clinic record and talk to you about the study to confirm you are eligible to participate. If you are eligible and agree, you will be asked to review and sign this consent form to take part. The consent discussion and brief questions will take 30 minutes to an hour.

During the main part of the study….

Study Procedures for Participants Assigned to Receive Standard Care

- If you are in the standard-of-care group, per your first randomization, you will continue to be seen by staff in the HIV clinic or other service location, like a drop-in centre, according to standard care guidelines recommended by the country's Ministry of Health and may choose to seek PrEP and PEP at a local health facility. There will be no change to your care.

- Data from your clinic records will be collected by study staff related to PrEP, PrEP, and other standard prevention methods, including when you were on PrEP/PEP, any HIV or sexually transmitted infections, and other details related to care or HIV prevention.
- You will also be seen for a study visit at the mid-point and end of the extension study (every 24 weeks) for HIV testing, including rapid and RNA tests, and a survey on what prevention method(s) you have been using. If you are currently using medications such as PrEP or PEP, you may be asked to provide hair, urine, or blood samples in order to measure the level of HIV prevention medications in your body. The results from tests measuring medication levels will not be shared, as this testing is for research only and will be performed in the future. The most blood drawn at a study visit will be about 1 tablespoon.

For SOC participants, Skip to the "Testing HIV-Positive" Section and Continue Consenting

Study Procedures for Participants Assigned to Continue to Receive Enhanced Services

- If you were assigned to receive the enhanced PrEP or PEP services, you will still receive these treatments according to standard care guidelines, but will also receive the services and procedures described below:
    i. Staff will discuss with you the integrated services offered in this study, described below. All your options will be discussed and questions answered. You will be provided a phone number of a study clinician that you can call any day of the week to start PEP immediately if you have had a recent exposure, or discuss any other urgent issue.
    ii. Study Visits: DCP Intervention Participants
        a. If you do not choose CAB-LA, you will return to clinic every 3-months for study visits and offered the DCP Package, as before.
        b. <u>PrEP or PEP:</u> you will take PrEP or PEP medications according to standard care guidelines recommended by the Ministry of Health, or have the option of HIV-testing only if you are not ready to start PrEP.
        c. You may switch between PrEP, PEP, CAB-LA, and frequent HIV-testing only at any time, according to your needs and the advice of your provider. At each visit, the HIV prevention method that is best for you will be discussed, with your options and preferences part of this continuing conversation. If new methods, such as the dapivirine vaginal ring, become available, these will also be offered as options. You may also have the option for a longer supply of PrEP medication or to use HIV self-testing.
        d. You will be asked questions on your attitudes on your choices of prevention and challenges at the start of the study extension and at the end of the study extension
    iii. Study Visits: CAB-LA Participants
        a. Once you choose to begin CAB-LA, you will be seen in clinic once a month for the first two months after the initial injection, then every 2-months for injections and your clinic study visits.

        b. SAPPHIRE staff will assist in scheduling and remembering these appointments

        c. If you are on CAB-LA, you can choose to stop at any time and switch to PEP, PrEP, or frequent HIV-testing only. Study staff will assist in the transition, so there are no gaps in prevention coverage

d. If you stop and would like to restart the injections, the study staff will assist in the timing of the injection restart, so there are no gaps in prevention coverage

e. You must come to clinic for the CAB-LA injection within +/- 7 days of your scheduled appointment: administration is not permitted off-site

f. If you cannot make it to clinic within the window for your next injection appointment, contact the SAPPHIRE study staff immediately to reschedule or to make arrangements for other prevention coverage

iv. All participants will come to clinic for the midpoint and closeout visits.

v. Staff will review with you any symptoms you may be having and refer you to other clinic services as needed. If staff think you have signs of recent HIV infection, a test will be ordered to rapidly measure any virus in your blood as an alternative way of testing for HIV.

vi. If there are challenges for you to access your oral medications, staff may deliver your PrEP or PEP medications and provide follow-up care at home or another location outside of the clinic that works for you. You may opt to change the location of the visit at any time during the study, including having phone visits. For any visits that take place at your home or other offsite location, staff will work with you to find a space that is private and where others cannot overhear the discussion or observe study procedures.

vii. Staff will also be available at any time to provide support if you have had any traumatic experiences or abuse at home or elsewhere, and will be trained to provide specialized counseling to help you manage these problems and help you find additional resources.

viii. Data from your clinic records will be collected by study staff related to PrEP, PrEP, CAB-LA, and other standard prevention methods, including when you were on PrEP/PEP/CAB-LA, any HIV or sexually transmitted infections, and other details related to care or HIV prevention.

ix. You will be seen for a study visit at the mid-point and end of the study for HIV testing, including rapid and RNA tests, and a survey on what prevention method(s) you have been using (every 24 Weeks). If you are currently using medications such as PrEP, CAB-LA, or PEP, you may be asked to provide hair, urine, or blood samples in order to measure the level of HIV prevention medications in your body. The results from tests measuring medication levels will not be shared, as this testing is for research only and will be performed in the future. The most blood drawn at a study visit will be about 1 tablespoon. Visits will take about the same amount of time as a regular clinic visit for people on PrEP or PEP. If you have discussions about your options or need additional testing, your visit may be an extra 30 or 45 minutes, as needed.

x. If you miss a visit, study staff may call you or visit you at your home. If you would not like to be visited at home or have a preference on the best way to be contacted, please tell the study staff.

<u>Long-Acting CAB General Overview</u>

1. If you choose the Long-Acting CAB option, you will continue having study visits similar to the quarterly visits in the DCP intervention. These will align with your CAB-LA injection visits.
    - If you choose to stop the CAB-LA injections, you will resume the DCP intervention as before, returning to clinic every three months for study visits and offered the original DCP Package.
2. At baseline, you will have a rapid HIV test and will proceed with the injection if negative. You will also have HIV-RNA testing, but will not have to wait for these results to receive the injection

3. At follow-up visits, you must have a negative HIV rapid test to proceed with the injection
4. You will have a health provider administer all injections. You will need injections every month for the first two months, and then every two months thereafter
    - You may choose to stop injections at any time
    - You may switch to PrEP, PEP, or HIV testing at anytime
    - Your study doctor will draw safety blood samples, such as ALT (Alanine transaminase) to test your liver health or check for Hepatitis B at the study start and during the study course at designated timepoints or per provider discretion
        - Participants found to have an Hepatitis B diagnosis will be discontinued from study

<u>Reasons you may have to stop taking the Long-Acting CAB injections</u>

There are some reasons you may have to stop taking CAB-LA:

- You experience a side-effect and it is no longer safe for you to take it
- The investigator determines that it is not safe for you to take it
- You get an HIV infection, which is explained further below

<u>Risks and/or discomforts:</u>

Most Common Side Effects:

- Pain, tenderness, hardened mass or lump, swelling, bruising, redness, itching, warmth, abscess, discoloration, or loss of sensation at the injection site
- stomach pain
- vomiting
- diarrhea
- muscle pain
- headache
- rash
- fever
- loss of appetite
- tiredness
- drowsiness
- sleep problems
- back pain
- nausea
- upper respiratory infection

Other side effects of cabotegravir may include:

a. Allergic reactions:
    - generally ill feeling
    - blisters
    - tiredness
    - muscle or joint aches
    - trouble breathing
    - fever
    - blisters or sores in the mouth
    - redness or swelling of eves
    - swelling of the mouth, face lips or tongues
b. Small increases in liver inflammation
c. Depression or Mood Changes

d. Hypersensitivity to Cabotegravir

If you experience any side effects, including those not mentioned above, contact your doctor immediately.

The shots you receive in this study are long acting, meaning they stay in your body for a long time – as long as a year or more. If you develop a side effect to CAB-LA after the shot, there will be no way to remove it from your body. If you get infected with HIV while on CAB-LA, it is possible that other HIV drugs that are like it may not work to fight the virus. The amount of CAB-LA in your body will decrease overtime and will eventually disappear.

Pregnancy and Breastfeeding:

Risks and Benefits

We have very little information on the safety of CAB-LA during pregnancy and breastfeeding You will need to weigh the risks to your pregnancy and infant to the benefits of your HIV prevention based on the information we have summarized below.

If you become pregnant during the study and choose to take CAB-LA during pregnancy, we will ask you to sign a separate consent form with more information, since pregnant women are excluded from enrolling in this study and we want you to make an informed decision about whether to continue.

If you are breastfeeding when you start this study or you breastfeed after becoming pregnant on the study and choose to begin CAB-LA, we want you to understand we have limited information on the safety of this drug during breastfeeding. We do know that in studies of another drug, called dolutegravir, which is very similar to CAB LA, no nursing babies had any problems. These babies were breastfed by mothers who had HIV and who were taking dolutegravir as treatment. Small amounts of dolutegravir were found in the breastmilk. It is possible some CAB LA may pass to a baby through breastmilk.

CAB LA has been detected in the blood circulation for up to 12 months or longer after an injection and the consequences of this level of exposure to the infant are currently unknown. Consideration should be given to the potential for infant exposure during pregnancy, even after the injections have been stopped.

- The safety of exposure of CAB- LA to infants through breastfeeding has not been established.
- Due to the nature of CAB-LA injections, CAB-LA may be present in breastmilk for up to, or beyond, a year after the final injection.
- The clinical consequences of exposure of the infant to CAB-LA are unknown.

While not required, to prevent any risk to the participant's pregnancy or to the infant, it is recommended that participants of child-bearing potential taking CAB-LA should use an effective contraceptive method, such as birth control (pills, intrauterine device, or implant) during the study, which can be obtained through standard care at the MoH. It is advised to continue using contraceptives through any additional extension phase and for 52 weeks (one year) after the last injection if stopping CAB-LA, to avoid pregnancy.

Storage and Shipment of Samples:
The hair, blood, and/or urine samples we may ask to collect from you to measure medication levels, confirm HIV infection, or test for resistance to HIV medicines will be stored at IDRC study facilities. Samples may be shipped to laboratories in the United States headed by researchers involved in the study: Dr. Monica Gandhi at UCSF in San Francisco or Dr. Urvi Parikh at the University of Pittsburgh. The samples will be stored for no

more than 5 years after the conclusion of the study and will only include study ID numbers as identifiers and will not include your name.

If these samples are requested, do you agree to have your samples collected and shipped to the laboratory in the United States for testing? If you decline this collection and shipment, you may still participate in other parts of the study.

Hair samples:

□ Yes _____ □ No _____
Participant's initials or thumbprint and date in space next to answer

Urine samples:

□ Yes _____ □ No _____
Participant's initials or thumbprint and date in space next to answer

Blood samples:

□ Yes _____ □ No _____
Participant's initials or thumbprint and date in space next to answer

When you are finished with the study (Week 48: Final Study Visit), ...
For intervention participants, your study doctor will assist with a transition plan to refer you to standard of care, ensuring no lapse in prevention coverage. For control participants, you will remain offered standard of care.

- Study Locations: This part of the study will take place in health centers and communities in Western Uganda and Western Kenya.

How long will I be in the study?

The program described in this consent form may last up to three years.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. They will tell you how to stop your participation safely.

Intervention participants: It is important to tell the study doctor if you are thinking about stopping so any risks from the PrEP/PEP/CAB-LA can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

All participants: If you withdraw from the study, any data or specimens we have already collected from you will remain part of the study records. After you withdraw, the researchers may still get information from your medical records if it is relevant to the study (e.g., laboratory results, treatment courses, health outcomes). You

must tell the study team you do not want this information to be collected when you withdraw, otherwise it will be collected.

The study doctor may stop you from taking part in this study at any time if they believe it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

Sensitive Discussions:
Some of the discussion about HIV and recent exposures may make you feel uncomfortable. If you feel uncomfortable with the topic under discussion, tell the study staff. If the discussion brings up instances of violence against you, including by a partner, family member or stranger, we will refer you to available resources for support or for reporting the event to the police. This is voluntary; it is up to you if you want to utilize such resources.

Confidentiality:
We will do our best to protect the information we collect from you, but confidentiality cannot be guaranteed and there is a small chance your information may be revealed. We will replace your name and all other identifying information with a unique code number on all study documents except those kept for contact information. There is a chance visits conducted at your home or other offsite location could be noticed by others, but we will work with you to find a private space in which to conduct the visit. Study-specific information will be stored in locked files, and only a small number of study staff will have access to it. You will not be identified in any report from this study. All information will be handled in compliance with Uganda and United States law for private information.

Hair Collection and Blood Drawing Risks:
If you are taking HIV prevention medicines like PrEP, CAB-LA, or PEP, a small hair sample may be collected (about 50-100 strands – the amount naturally lost each day). The hair sample will be collected from the back of the scalp using a clean pair of scissors in a process that takes 90 seconds. There is a potential but low risk of cutting the skin with the scissors. If you are suspected to have recently been exposed to HIV, a blood sample may be drawn by study staff to detect any HIV virus that may be in the blood. Taking blood may cause brief discomfort and bruising. Infection or fainting can happen but are rare.

Risks from taking CAB-LA:

<u>Risks and/or discomforts:</u>

Most Common Side Effects:

- Pain, tenderness, hardened mass or lump, swelling, bruising, redness, itching, warmth, abscess, discoloration, or loss of sensation at the injection site
- stomach pain
- vomiting
- diarrhea
- muscle pain
- headache
- rash
- fever
- loss of appetite
- tiredness
- drowsiness

- sleep problems
- back pain
- nausea
- upper respiratory infection

Other side effects of cabotegravir may include:

e. Allergic reactions:
    - generally ill feeling
    - blisters
    - tiredness
    - muscle or joint aches
    - trouble breathing
    - fever
    - blisters or sores in the mouth
    - redness or swelling of eves
    - swelling of the mouth, face lips or tongues
f. Small increases in liver inflammation
g. Depression or Mood Changes
h. Hypersensitivity to Cabotegravir

Are there benefits to taking part in this study?

There will be no direct benefit to you from participating in this study. The enhanced measures to improve PrEP and PEP delivery, if you are assigned to the group that receives it, may help you stay on medications, receive care, or reduce the likelihood of acquiring HIV infection, but this cannot be guaranteed. Your participation in the study may benefit the community, scientists and doctors who work on providing HIV care in health centers such as yours.

What other choices do I have if I do not take part in this study?

You do not have to participate in this study. Your other choices may include:

- You can be put on to the national standard of care for HIV prevention. Your access to PrEP and PEP through the clinic will not be affected if you decide to stop participating in the study.

Are there any costs to me for taking part in this study?

No. The sponsor has agreed to pay for all items associated with this research study; you or your insurer will not be billed.

Will I be reimbursed for taking part in this study?

In return for your time and effort, you will be receiving a reimbursement of 20,000 Uganda shillings to offset the cost of travel and time for participating at Weeks 0, 24, and 48.

Will I be compensated for taking part in this study?

You will not be compensated for taking part in this study.

How will my information be used?

Researchers will use information to conduct this study. Once the study is done using your information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

How will information about me be kept confidential?

Care will be taken to protect your privacy. Study participants will be identified only by their unique code number on all study documents except those kept for contact information. All information will be handled in compliance with Uganda and U.S. law for confidential information. The Makerere School of Medicine Research Ethics Committee (SOMREC) and Uganda National Council for Science and Technology (UNCST), which are institutions that oversee human research, may have access to study information that may have your name. In addition, authorized representatives from the National Institutes of Health and University of California may review your research data for the purpose of monitoring or managing the conduct of the study. Besides these institutions, the universities and research organizations running this study are not allowed to let others know the identity of the people in the study.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

What happens if I am injured taking part in this study?

It is important that you tell the study doctor, Dr. Moses Kamya, at 075-2-900012, if you feel that you have been injured because of taking part in this study.

Who can answer my questions about the study?

If you have any questions about this study, including those about research-related harm, please contact the lead investigator in Uganda, Dr. Moses Kamya, at 075-2-900012. You may also contact Assoc. Prof Ponsiano Ocama, the chair of the Makerere University School of Medicine - Research and Ethics Committee in Uganda at 077-2-421190, which approved this study, for questions about participants' rights and research-related harm.

In addition, a description of this study will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. After the study is over, this website will include a summary of its results

CONSENT: WHAT YOUR SIGNATURE OR THUMBPRINT MEANS

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw from participation at any point in this study without penalty or loss of benefits to which you are otherwise entitled. A copy of this consent form will be given to you. Your signature or thumbprint below means that you have had this study explained to you. Your signature or thumbprint below means you have had the opportunity to ask questions and get answers. If you wish to participate in this study, you should sign or place your thumbprint below.

Name of Participant (printed)

Signature or Fingerprint* of Participant Date

Name of Study Staff Administering Consent (printed) Position/Title

Signature of Study Staff Administering Consent Date

Name of Translator (if necessary)

Signature of Translator Date

*If the participant is unable to read and/or write, an impartial witness must be present during the consent discussion. After the written informed consent form is read and explained to the participant, and after he or she has orally consented participate in this study, and has either signed the consent form or provided his or her fingerprint, the witness must sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given.

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date