maple leaf research

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Participant Information and Informed Consent Form

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Protocol Title: Drug-drug interaction study between bictegravir/emtricitabine/ tenofovir alafenamide and feminizing hormones in trans women living with HIV

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Please Read This Document Carefully

You are invited to be in a research study because you are 18 years of age or older and:

- A trans woman living with HIV and is currently taking oral estradiol and the HIV medication (Antiretroviral Therapy (ART)) Biktarvy® or is willing and able to switch to it.
  OR
- A cis woman living with HIV currently taking the HIV medication (ART) Biktarvy® or is willing and able to switch to it and of reproductive age with:
  - Regular periods (a period every 24-35 days) or,
  - If periods are irregular due to being on a progesterone only contraceptive (ex. Mirana) or,
  - If periods are absent due to your uterus being removed (hysterectomy) but your ovarie(s) remain functional

  OR
- A trans woman living without HIV and is currently taking oral estradiol.

For the purpose of this study, a trans woman is a person who was assigned male sex at birth and currently identifies as a woman. Trans women can be at any stage of medical, social, or legal transition but must have been taking an oral estradiol for the last 6 months and an antiandrogen (unless medically /surgically not necessary). A cis woman is a person who identifies as a female and is the same as the sex (female) they were assigned to at birth.

Taking part in a research study is voluntary. Before you decide, you should know why the research is being done and what it involves. Please read this form carefully and take your time to decide. Ask the study doctor or referring doctor (or their staff) any questions you may have. You may take an unsigned copy of this form home with you to read again. Take your time to think and talk about it with your family and friends before making your decision. Being in a research study is not part of your routine medical care.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as recommended by Health Canada. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What is a Clinical Research Study?

A research study is a way of getting new information on a treatment, diagnostic test, or something else health related. Research studies help us to answer questions about something that is not well understood.

This Participant Information and Informed Consent Form explains the study to you. Your study doctor or study staff will go over this form with you, and they will answer all the questions you have about this research study.

If you agree to participate, you will be asked to sign and date this form. You will be given a signed and dated copy to keep. Taking part in this study is completely voluntary, meaning no one can force you to participate in this study. Even if you agree to participate now, you can change your mind and stop at any time without penalty or loss of benefits which you would otherwise be entitled.

Why is this study being done?

There have been tremendous advances in the care of trans women living with human immunodeficiency virus (HIV), with various medical and surgical treatment options becoming more available and safer. However, there is not a lot of information available about what happens in the body when feminizing hormone therapy (medications trans women sometimes use) and HIV Medications (Antiretroviral Therapy (ART)) are taken together. Since there is not a lot of information available, some trans women living with HIV feel that they must choose between taking their feminizing hormone therapy (FHT) and their HIV Medications when they need or desire both.

The purpose of this study is to understand if taking feminizing hormone therapy and HIV medications (ART) together will cause the drug level of either of these medications to increase or decrease. This is called a drug-drug interaction (DDI) and we only know if it happens when we test the drug levels in people's blood. From this study, we will find out if there are any drug-drug interactions and what happens to your estradiol hormone levels and HIV medication levels (if applicable) in your blood over a 24-hour period. This information will be determined using laboratory testing.

Other purposes of this study are to assess satisfaction with medical gender affirmation (the use of feminizing hormone therapy) for trans women and ART for women living with HIV through questionnaires. Adherence (whether you take your pills as prescribed), adverse events, and patient-reported outcomes to Biktarvy® and health status will also be assessed. Additionally, the number of participants with an undetectable viral load will also be determined using laboratory testing.

Who will participate in this study?

We are enrolling 45 women 18 years of age or older into this study:

- 15 trans women living with HIV on oral estradiol and Biktarvy® or another ART
- 15 cis women living with HIV on Biktarvy® or another ART and of reproductive age with:
    - Regular periods (a period every 24-35 days) or,

  - If periods are irregular due to being on a progesterone only contraceptive (ex. Mirana) or,
  - If periods are absent due to uterus being removed (hysterectomy) but ovaries(s) remain functional),
- 15 trans women living without HIV on oral estradiol

The study will be conducted through Maple Leaf Research in Toronto. Visits can be a combination of virtual and in-person visits. However, the Month 2 visit must be conducted in person.

The following clinics are recruiting participants:

- Maple Leaf Medical Clinic, Toronto
- Sherbourne Community Health Centre, Toronto
- St. Michael's Department of Family and Community Medicine at Unity Health in Toronto
- Church-Wellesley Clinic, Toronto
- Dr. Raymond Fung's endocrinology clinic, Toronto
- Women's Health in Women's Hands
- 790 Bay St. Clinic

What drugs are being used in this study and how will they be provided?

In this study, we are evaluating the drug-drug interactions between Biktarvy®, an HIV medication (ART) and an oral estradiol, a type of feminizing hormone:

1) **For participants living with HIV:**
   Biktarvy®:

   - Biktarvy® is a widely available single tablet regimen (one pill a day) that is approved by Health Canada to treat HIV.

   - Participants will take Biktarvy® orally, once a day (in the morning) with or without food until you complete the Month 6 Visit. However, if preferred after the Month 2 visit Biktarvy® can be taken in the evening.

   - Recommendations for taking Biktarvy®:
     - If you take antacids that contain aluminum or magnesium, take Biktarvy® at least 2 hours before or after you take these antacids.

- If you take supplements or antacids that contain iron or calcium, take Biktarvy® with food at the same time that you take these supplements or antacids.

- Participants living with HIV will either already be taking Biktarvy® or will need to switch to it for the duration of the study:
  - If you need to switch from another ART to Biktarvy®, this will happen at the Baseline visit.
    - If you are taking the ART at night, you will need to switch to taking it in the morning the day after the screening visit until the Baseline visit. You will be asked to do so after you sign the consent form.
      - Unless you are taking Atripla (which is taken at night) where you can continue to take it at night until the Baseline visit.
    - You will switch from the other ART to Biktavy® at the Baseline visit, the drug will be provided at no cost by Gilead Sciences for the duration of the study (6 months).
  - If you are already on Biktarvy® and you are taking it at night, you will need to switch to taking it in the morning the day after the Screening visit until after the Month 2 visit. You will be asked to do so after you sign the consent form.
    - You will be required to obtain your own Biktarvy (if applicable) as you have been doing until now. If you are not 100% covered, please contact the study team for assistance.
    - After the Month 2 visit if you prefer you may switch back to taking Biktarvy® at night.

2) **For trans women participants:**
Oral estradiol:

- Oral estradiol is the most commonly used feminizing hormone in Canada as it is the only estrogen therapy covered by provincial drug plans.

- If you are taking more than 2 mg estradiol, will need to split your dose to twice a day (2 mg in the morning and the rest of the dosing in the evening). You will be asked to do so after you sign the consent form.

- If you only take 2mg estradiol once daily, you will need to switch to taking it in the morning (if applicable).

- If you are currently crushing or taking your oral estradiol sublingually (under the tongue), you will need to swallow the pill for the duration of the study. You will be asked to do so after you sign the consent form.

- You need to take your oral estradiol as explained above until after the month 2 visit is complete.

- You must continue to take your anti-androgen daily until after the month 2 visit is complete (if medically needed).

- You cannot take any estrogenic therapies (including herbal hormone supplements) other than your prescribed feminizing hormone regimen.

- You will be required to obtain your own oral estradiol as you have been doing until now. If you need to switch your dosing schedule, the study doctor will provide a new prescription.

We ask that any use of over-the-counter medications, prescription medications, or natural health products be reported to our study team.

What about birth control and pregnancy during the study?

You are not eligible to participate in this study if you are taking any estrogen or conjugated estrogen containing birth control products (ex. NuvaRing, Plan B, Ortha Evra). Non-estrogen containing products such as copper IUDs, Mirena, and Depo-Provera can be used as birth control. If you are unsure if the birth control you are taking is allowed please ask the study staff.

You are not eligible to participate in this study if you are pregnant or plan on being pregnant within the duration of the study. Serum (blood) pregnancy tests will be completed at each visit and an additional urine pregnancy test will be completed at the Month 2 visit to confirm that you are not pregnant. If you become pregnant prior to the Month 2 visit, you will be withdrawn from the study, and we will recruit another participant in your place.

How long will I be in the study?

The screening window (time between starting the study and baseline) will be approximately 15 -30 days but could be up to 90 days.

For participants living with HIV, you will be in the study for 6 months plus the screening window and will have 4 visits in total (Screening, Baseline, Month 2, and Month 6). If you need to switch to Biktarvy, you will have an extra visit at Month 1.

For participants living without HIV, you will be in the study for 2 months plus the screening window and will have 3 visits in total (Screening, Baseline, and Month 2).

- The Screening and Baseline Visit can be done virtually.
- The Month 1 Visit will be a standard of care visit for participants that switch their ART regimen to Biktarvy®; it can be done virtually.

- The Month 2 Visit is completed over 24 hours- 2 days.
- You will arrive in the morning (between 7:30AM-10:30AM) on both Day 1 & Day 2.
    - On Day 1 you will be at the clinic for about 8.5 hours.
    - On Day 2 you will only need to do 1 blood draw prior to taking your medications and you will be at the clinic for about 30 minutes.
- The Month 6 Visit is only required for woman living with HIV ; it can be done virtually.
- Requisitions for any blood samples needed for visits done virtually will be sent to your email and can be done at any local LifeLabs® (https://locations.lifelabs.com/locationfinder). The requisitions can also be faxed to LifeLabs®.

What will happen during the study?

If you agree to participate this study, you will first either come to the clinic at Maple Leaf Research (14 College Street, Suite 403, Toronto, ON) or have a virtual Screening Visit to sign the consent form and see if you are eligible to participate. If you are eligible to participate, you will be asked to come back to the clinic for one to five study visits (as explained above).

We will have a community member available for support at Maple Leaf Research during your baseline and Month 2 visit. You can also bring a friend to your visits.

The number of visits and the procedures will vary depending on your group.

See the tables on the following pages for procedures per visit for the corresponding groups:

- Trans woman living with HIV currently taking oral estradiol and Biktarvy® or are willing and able to switch to Biktarvy® **(Group 1).**
- Cis woman living with HIV currently on Biktarvy® or are willing and able to switch to Biktarvy® **(Group 2).**
- Trans woman living without HIV currently taking oral estradiol **(Group 3).**

No genetic testing will be done as part of this study.

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Group 1 Visits and Procedures- 15 Trans Women living with HIV

Screening	Baseline	Month 1	Month 2	Month 6
Review and sign consent form Confirm eligibility: • Medical history and medications review • Demographic Questionnaire ***Lab Sample:*** • HIV viral load • HBV/HCV Serology • Urine protein Switch ART to morning (if applicable) Change FHT dose to morning & start swallowing the pill (if applicable) Split FHT dosage (if applicable) Receive $40	**(7:30 – 8:30 AM start)** Breakfast provided (if done in person) Biktarvy® and Estradiol Meds Taken ***#1- Lab Samples:*** • HIV viral load & CD4 • Routine Bloodwork • Urine protein • Testosterone & Estradiol levels Height & Weight Doctor visit (if needed, the most common reason a doctor visit may be requested would be clarification of any changes in medication). Questionnaires: • FEM-SQ • Adherence • HSDIM PRO • HIVTSQs • SF-36 ***#2-Lab sample** (4H after meds taken):* • Estradiol level Switch to Biktarvy® from your current HIV meds (if applicable): Switched to Biktarvy® → Already taking Biktarvy® → Receive $80	Virtual Standard of Care Visit to be completed **ONLY IF** switched to Biktarvy®. Doctor follow-up Questionnaire: • Adherence Receive $20	**Day 1: (7:30 – 8:30 AM start)** Breakfast provided Biktarvy® and Estradiol Meds Taken ***#1- Lab Sample:*** • HIV viral load • Routine bloodwork • Testosterone & Estradiol levels • Biktarvy® levels Weight Questionnaires: • FEM-SQ • Adherence • HSDIM PRO • HIVTSQs • SF-36 ***Over 24 hours:*** ***Nine (9) Lab Samples collecting Biktarvy® Levels:*** 0.5, 1, 1.5, 2, 3, 4, 6, and 8 hours after meds ***Seven (7) Lab Samples collecting Estradiol Levels:*** 1, 2, 3, 4, 6, and 8 hours after meds PBMC and Dried Blood Spot 2 hours after meds Receive $160 (Day 1) (Lunch will be provided on Day 1) **Day 2: (7:30 – 8:30 AM)** ***Lab Sample:*** (before you take Meds) • Estradiol & Biktarvy® level Receive $40 (Day 2)	***Lab Sample:*** • HIV viral load & CD4 • Routine bloodwork Doctor follow-up (if needed) Questionnaires: • FEM-SQ • Adherence • HSDIM PRO • HIVTSQs • HIVTSQc • SF-36 Receive $50 Switch back to original regimen (if preferred)

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Group 2 Visits and Procedures- 15 Cis Women living with HIV

Screening	Baseline	Month 1	Month 2	Month 6
Review and sign consent form Confirm eligibility: • Medical history and medications review • Questionnaires: Demographic Menses history ***Lab Sample***: • HIV viral load • Pregnancy test (serum) • HBV/HCV serology • Urine protein • FSH test Switch ART to morning (if applicable) Receive $40	**(7:30 – 8:30 AM start)** Breakfast provided (if done in person) Biktarvy® Taken ***Lab Sample:*** • HIV viral load & CD4 • Routine bloodwork • Urine protein • Testosterone & Estradiol levels • Pregnancy test (serum) Height and Weight Doctor visit (if needed) Questionnaires: • Adherence • HSDIM PRO • HIVTSQs • SF-36 • Menses history Switch to Biktarvy® from your current HIV meds (if applicable): Switched to Biktarvy® → Already taking Biktarvy® → Receive $50	Virtual Standard of Care Visit to be completed **ONLY IF** switched to Biktarvy®. Doctor follow-up Questionnaire: • Adherence Receive $20	**Day 1: (7:30 – 8:30 AM start)** Breakfast provided Biktarvy® Taken ***#1- Lab Sample:*** • Pregnancy test (serum & urine) • HIV viral load • Routine bloodwork • Testosterone & Estradiol levels • Biktarvy® level Weight Questionnaires: • Adherence • HSDIM PRO • HIVTSQs • SF-36 • Menses history ***Throughout the day:*** ***Nine (9) Lab Samples collecting Biktarvy® Levels:*** 0.5, 1, 1.5, 2, 3, 4, 6, and 8 hours after meds PBMC and Dried Blood Spot 2 hours after meds Receive $160 (Day 1) (Lunch will be provided) **Day 2: (7:30- 8:30 AM)** ***Lab Sample:*** (before you take Meds) • Biktarvy® level Receive $40 (Day 2)	***Lab Sample:*** • HIV viral load & CD4 • Routine blood work • Pregnancy test (serum) Doctor follow-up (if needed) Questionnaires: • Adherence • HSDIM PRO • HIVTSQs • HIVTSQc • SF-36 • Menses history Receive $40 Switch back to original regimen (if preferred)

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Group 3 Visits and Procedures- 15 Trans Women living without HIV

Screening	Baseline	Month 2
Review and sign consent form Confirm eligibility: • Medical history and medications review • Questionnaire: Demographic ***Lab Sample:*** • HIV test • HBV/HCV Serology Change FHT dose to AM & start swallowing the pill (if applicable) Split FHT dosage (if applicable) Receive $40	**(7:30 – 8:30 AM start)** Breakfast provided (if done in person) Estradiol Taken ***#1- Lab Sample:*** • HIV test • Routine Bloodwork • Testosterone & Estradiol levels Doctor follow-up Height and Weight Questionnaires: • FEM-SQ • HSDIM PRO • SF-36 ***#2- Lab Sample*** *(4H after meds taken)* • Estradiol level Receive $80	**Day 1: (7:30 – 8:30 AM start)** Breakfast provided (if done in person) Estradiol Taken ***#1- Lab Sample:*** • HIV test • Routine bloodwork • Testosterone & Estradiol levels Height and Weight Questionnaires: • FEM-SQ • SF-36 ***Over 24 hours:*** ***Seven (7) Blood Samples collecting Estradiol Levels:*** 1, 2, 3, 4, 6 and 8 hours after meds Receive $160 (Day 1) (Lunch will be provided) **Day 2: (7:30- 8:30 AM)** ***Blood Sample*** (before you take Meds): • Estradiol level Receive $40 (Day 2) Switch back to original regimen (if preferred)

What are the types of tests and procedures that are being done for this study?

Please see the table below for a description of all the tests and procedures that are being completed during this study.

Procedure or Test	Description
Medical history and medications review	Demographics (e.g. age, race, education, etc.(questionnaire) screening only; medical history (e.g. FHT history, HIV history, menses history questionnaire, etc.) and medication history (e.g. gender affirming surgery, chronic ongoing conditions, psychiatric, major medical conditions); feminizing hormones, hormonal contraception, medications used to treat or prevent HIV, herbal/over-the counter medication, and any other medication used in the 30 days prior to screening). This is done to confirm your study eligibility. The medical and medication history is updated at each visit as required.
Doctor Visit & Physical Exam	A doctor visit and/or physical exam will only be done if deemed medically necessary by the study personnel. The most common reason would be if you need to switch to Biktarvy or change your estradiol dose. You will be booked with a study physician to get a new prescription, follow-up on any side effects or clarify changes in medication. Month 1 visits will require a doctor visit as these participants will have switched to Biktarvy.
Routine Blood Tests (standard of care tests)	Samples of your blood will be tested to check your health. If any of the test results are abnormal, your study doctor may ask you to come for repeat testing. Routine blood work includes CBC, electrolytes [sodium, chloride, potassium], serum creatinine [eGFR], ALT, total bilirubin, glucose, HbA1C and lipids.
Serum and Urine Pregnancy Tests	Serum pregnancy tests will be done for cis women at every visit with an additional urine pregnancy test done at the Month 2 visit to confirm that they are not pregnant and continue to be eligible for the study.
Urine Protein	For women living with HIV, a urine sample will be collected at screening and baseline visit to check your health.
Hepatitis B and Hepatitis C Virus Test	Blood samples will be taken to test for the presence of Hepatitis B and Hepatitis C viruses done through the public health lab at screening only.
HIV-1 serology test	HIV negative women will have an HIV blood test done through the public health lab to confirm their HIV negative status at all visits.
HIV -1 RNA Viral Load	For women living with HIV, a blood sample will be collected and sent to the public health lab to determine the level of virus in your blood.

Procedure or Test	Description
Lymphocyte Subset CD4 + CD8	For women living with HIV, a blood sample will be collected and sent to the public health lab to get your CD4 and CD8 levels- this is a specific white blood cell in your immune system, that is targeted by the HIV Virus.
Testosterone Level	A blood sample will be collected to measure the testosterone level in your blood. This will be sent to LifeLabs® for processing. This test will only be done during the Baseline and Month 2 visits.
Estradiol Levels	Blood samples will be collected at varying times during the Baseline and Month 2 visits to determine your estradiol levels in your body. At the Month 2 visit they will be collected over a 24H period. They will be sent to LifeLabs® for processing.
HIV drug levels Peripheral blood mononuclear cells (PBMC)	For women living with HIV: This is a special blood test looking at specific cells in your body called peripheral blood mononuclear cells. This test has a very specific way to process and store these blood samples to make sure your levels of Biktarvy® can be tested properly. No genetic testing will be done with these samples.
Blood samples for ART drug levels (PK- pharmacokinetics)	For women living with HIV: Blood samples will be collected at varying times during the Month 2 visit to determine the levels of Biktarvy® in your body over a 24H period.
Dried Blood Spot (DBS) test	Blood samples will be collected at varying times during your visits to determine the levels of Biktarvy® in your body. A drop of blood will be put on a paper card and dried before freezing. No genetic testing will be done with these samples.
Questionnaires	Description
Demographics	You will be asked some questions regarding your demographics (e.g., age, employment status, etc.) and medical history (e.g., past health conditions, smoking status, medications, etc.)
Menses History	You will be asked some questions regarding your menses history.
FEM-SQ	The Feminizing Medical Gender Affirmation Satisfaction Scale.
Adherence Assessment	The purpose of this is to assess your adherence to taking your ART medications.
HSIDM Questionnaire	HIV Symptom Index Distress Module. This is to assesses the burden of 20 common symptoms associated with HIV treatment or disease.
HIVTSQ Questionnaires	HIV Treatment Satisfaction Questionnaire
SF-36 Questionnaire	Short Form 36 (SF-36) that assesses quality of life.

What do I have to do?

If you decide to participate in the study, you will have some responsibilities:

- You must come to the clinic in the morning (approx. between 8:30a.m.-10:30a.m.) for both Day 1 and Day 2 of the Month 2 study visit; the other visits can be done virtually.
- You must follow the information sheets and any instructions you are given by the study staff.
- You must take your feminizing hormones and/or ART medication **in the morning** as directed by the study staff.
- You must share the required information about your health with study staff.
- You must tell the study staff about any medications you are taking or start throughout the study.
- You must not take the following medications while in the study:
    - Medication to prevent HIV -- Pre or Post Exposure prophylaxis (PrEP / PEP).
    - Any herbal hormone replacement medication (such as St John's Wort).
- You must avoid drinking Grapefruit juice while in the study.

- For the Baseline*/ Month 2 visits:
    - You need to arrive at the clinic in the morning between 7:30-10:30AM, **prior to taking** your feminizing hormones and HIV medications (if applicable).
        - *The Baseline visit can be conducted virtually, where the requisitions for blood work will be sent to you to complete at a nearby LifeLabs®.
    - You will need to be fasting [that means no food or drinks (except water) for 10H].
    - We will provide you with breakfast at Baseline (if done in person) and the Month 2 visits.
    - If you are living with HIV, you must take your ART **in the morning** during the study.
    - If you switch your HIV medication to Biktarvy®, you will be provided with Biktarvy® at the Baseline visit for the duration of the study (6 months) and you will attend a virtual Month 1 standard of care visit.
    - For the Month 2 Visit - you will need to stay at the clinic (or near the clinic) for about 8.5 hours and then return again the next morning at the same time as Day 1 before taking your medications.
        - A community support member will be at this visit with you.
        - Lunch and snacks will be provided at this visit.
    - Women living with HIV will return to the clinic for a Month 6 visit. This visit can also be done virtually.
        - If you changed to Biktarvy® for the study, you can switch back to your old medication if you would prefer after this visit.
    - If you are unsure about what you are supposed to do, ask the study staff or your study doctor.

You may be removed from the study if your responsibilities are not met.

Note: There could be other rules that your study doctor will review with you.

How much blood will I be asked to provide?

Please see the table below for the approximate amount of blood to be collected at each visit:

	Screening	Baseline	Month 2	Month 6
Group 1	12-18 mL	28-32 mL	142 mL	20 mL
Group 2	18-24 mL	28 mL	112 mL	26 mL
Group 3	18 mL	28-32 mL	58 mL	N/A

Month 2 Visit Repeat

If for any reason the required blood samples could not be collected at the Month 2 visit, the collection of blood samples for the Month 2 visit will be repeated if the principal investigator thinks it's necessary. The procedures for the day will be the same:

1. You will need to come in fasting for 10 hours prior to the visit (bring your medication with you).
2. We will serve you breakfast (350-500 calories).
3. Draw a pre-dose sample of estradiol, testosterone and ART.
4. Take your medication within 30 minutes of breakfast
5. Then blood will be drawn at 0.5, 1, 1.5, 2, 3, 4, 6 and 8 hours after taking your medications.
6. You will need to come back the next day for the 24-hour blood sample to be drawn.

What are the potential risks to participating in this study?

- ***Bloodwork:***
    - The risks associated with this procedure may involve a small amount of bleeding when blood is taken and there may be slight discomfort or lightheadedness, swelling, pain, bruising or redness where the needle pierces the skin. In very rare cases, fainting or infection can occur.

- ***Questionnaires:***
    - Some of the questions are personal and there is a possibility that questions related to body positivity and the effects of feminizing hormones might be upsetting to you. If you have any questions or concerns while answering these questions, please talk to your study doctor. Information about The 519 (a city organization dedicated to advocacy for the inclusion of LGBTQ communities in Toronto) and other local counselling services will be provided based on the medical professionals' judgement and/or at your request.

- ***Medication:***
    - A few risks are associated with taking Biktarvy® for people living with HIV-1. The only absolute contraindication to the drug is a known hypersensitivity to the drug itself. Severe acute exacerbations of hepatitis B have been reported in patients co-infected with HIV-1 and HBV, and it may occur with discontinuation of Biktarvy®.
    - From clinical studies very common (more than or equal to 10%) side effects seen were headache, and diarrhea. Other common (> 1% and <10%) side effects were nausea, vomiting, abdominal pain, indigestion, passing gas, fatigue, and rash.
    - If you have changed your estradiol dose or switched to Biktarvy, you can be booked with a physician to get a new prescription and/or to follow-up on side effects. If you feel any side effects or unusual symptoms, please notify your study doctor as soon as possible at the phone number listed in this form.
    - A few risks are associated with taking estradiol. These risks include venous thrombosis/thromboembolism, increased risk of cardiovascular disease, weight gain, decreased libido, hypertriglyceridemia, elevated blood pressure, decreased glucose tolerance, gallbladder disease, benign pituitary prolactinoma, mental health effects and infertility.
    - Women rarely have severe side effects from taking estradiol. The most common are abdominal pain, nausea and vomiting. Other possible side effects are depression, nervousness, and/or irritability, allergic reaction and rash, increased blood sugar levels, change in blood pressure, acne, change in cholesterol and/or triglyceride levels, change in weight.
- ***Other:***
    - During the pandemic period (COVID-19), if you or your study doctor are unable to complete study visits in the clinic, we will ensure your Biktarvy® (if applicable). If the study visit is not completed in the clinic in a timely manner, your study doctor can assess your health status virtually.
    - There is the potential risk of re-identification (in relation to the data). Although this may be unlikely to occur, the potential risks are significant given the study population, and it is important to ensure that all participants are well aware of this possibility. Despite protections being in place, there is a risk of unintentional release of information. We will do everything we can to limit this risk, such as by assigning a participant ID to your personal information. If your screening visit is done virtually, the consent form can be signed electronically.

What are the potential benefits to participating in this study?

You likely will not experience direct benefit from participation in this study. However, you will be supporting the development of knowledge on drug-drug interactions between feminizing hormones and HIV medications. This is important information for trans women living with HIV; the study was inspired by a working group of trans women- the Trans Women HIV Research Initiative (TWIRI) who identified a lack of scientific information about drug-drug interactions between feminizing hormones and HIV medications.

For more information, please visit: https://www.transwomenhivresearch.com/

Are participants paid to be in this study?

If you decide to participate you will receive a compensation at the end of each visit completed as follows:

Visit / Group	Screening	Baseline	Month 1	Month 2 (Day 1)	Month 2 (Day 2)	Month 6
Group 1	$40	$80	$20	$160	$40	$40
Group 2	$40	$50	$20	$160	$40	$40
Group 3	$40	$80		$160	$40	

- These honoraria will be provided to cover out of pocket expenses for your participation in this study (e.g., transportation, meals, childcare, inconvenience, etc.).
    - We will provide breakfast during the Baseline visit (if done in person), and breakfast, lunch and snacks during the Month 2 visit.
    - If you would like to bring a support person with you for the Month 2 Visits, we will provide that person with breakfast, lunch, and an honorarium of $50.
- If you are travelling to the study site for the Month 2 visit, because you live outside of the GTA (Greater Toronto Area), you will also be reimbursed for reasonable transportation, hotel, and meal allowance. This will need to be pre-approved by the study team. Receipts need to be provided to the study site for reimbursement.
    - Please discuss these costs with the study staff prior to planning your travel.

How much will study treatment cost you?

- All study visits and drug level tests that are part of this study will be provided at no cost to you. You or your usual health care payer will be responsible for any other health care costs.
- You will be required to obtain your own oral estradiol (if applicable) as you have been doing until now.

- You will be required to obtain your own Biktarvy® (if applicable) as you have been doing until now. Speak to the study team if you need any assistance.
- If you switch to Biktarvy® at the baseline visit, Biktarvy® will be provided to you free of charge for the duration of the study.

Participation and Withdrawal

- Your decision to participate in this research study is entirely voluntary. You may decide to not be part of this study, or to be in the study now and then change your mind later. You may withdraw from the study at any time without it affecting your medical care. If you decide to leave this study early, we will ask you if you would like your data to be destroyed, or if the data collected can be used in this study.
- If you no longer want your data to be used in this research study, you should tell the study doctor who will ensure the data is removed. However, if you withdraw your consent after the data is analyzed, the test results and research study information must remain in any database(s) that were created for the research study as the results will be in the public domain (i.e. published and presented in national and international conferences).
- A study doctor may remove you from the study at any time without your consent for any of the following reasons: if it appears to be medically harmful to you; if you fail to follow directions for participating in this study; if it is discovered that you do not meet the study requirements; at the discretion of the study doctor or if the study is cancelled.

Research Information in Shared Clinical Records

- If you participate in this study, information about you from this research project will be stored in the secure Electronic Medical Record (EMR) system at Maple Leaf Medical Clinic (Toronto). This data on the EMR is confidential.
- Information taken from the EMR will be de-identified (by replacing participant names with participant ID numbers) before being entered into a secured research database. If desired, the study team can review which information about you will be stored electronically and may be shared outside of Maple Leaf Research/Maple Leaf Medical Clinic.
- Identifiable information will be accessed by the research staff through the EMR system to contact the patient for scheduling purposes, access medical history to ensure eligibility, as well as, to receive and input lab results.
- If you have any concerns about this, or have any questions, please contact:
    - Roberta Halpenny Research Manager of Maple Leaf Research, roberta@mlmedical.com
    - Dr. Megan Acsai, Maple Leaf Medical Clinic Privacy Officer, at 416-966-9441.
- A secure electronic database will be used to store the data for this study. This database will be stored on secure servers at the Canadian Institutes of Health Research (CIHR) Canadian HIV Trials Network. You will be identified in the database by your study ID. The link between your

personal study ID and identifying information will remain on a log which will be securely stored at Maple Leaf Research. All paper study materials will be kept in a binder behind protected/locked doors and in a locked cabinet. Other digital files will be restricted to study personnel and will be kept on secure servers. All study materials will be kept for 15 years before destruction as per Health Canada standards. All medical health information collected in the Electronic Medical Records (such as your visit records or laboratory results) and assigned to your name will be stored according to clinical policies and provincial legislation.

- Please note that the security of e-mail messages is not guaranteed. Messages may be forged, forwarded, kept indefinitely, or seen by others using the internet. Do not use e-mail to discuss information you think is sensitive. Do not use e-mail in an emergency since e-mail may be delayed.

How will my privacy be protected?

- If you decide to participate in this study, the study staff will only collect the information they need for this study. Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.
- It is possible to sign this document electronically, once signed by both parties, we will both receive a copy by email. We will then delete the signed copy from the program, but we will keep a paper copy of the signed document in your study file.
- Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines:
    - *Dr. Mona Loutfy*, the Principal Investigator of this study;
    - *Dr. Ian Armstrong,* Co-Investigator of this study;
    - *Roberta Halpenny, Tigist Kidane, Geraldine Tuason, Sonca Legnoc,* the research staff for Maple Leaf Research; there may also research assistants.
    - *Representatives of Veritas IRB,* the research ethic board who oversees the ethical conduct may review the study you are participating in for quality assurance to make sure that the required laws and guidelines are followed. All information accessed by Veritas IRB will be upheld to the same level of confidentiality that has been stated by the research team.
- This research study is collecting information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence drug levels and how people respond to questions. Providing information on your race or ethnic origin, and any other question, is voluntary.
- It is expected that the information collected during this study will be used in analyses and will be published/presented to the scientific community at meetings and in journals. If the results of this

study are published, your identity will remain confidential. We will not use your name in these publications/presentations.

- Because this study includes a small number of participants who are potentially identifiable, we will do our best to limit the amount of information presented to mitigate the risk of you being identified; one way this is done is to present the data for the group as a whole, never from one individual person. Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

Publication of results

Once the study is completed and the information is verified and analyzed, the results will be published and presented at national and international conferences and to community groups as appropriate. Also, infographics (diagram), fact sheets and community reports will be provided to help support trans women living with HIV to understand the findings and issues with DDIs between ART drugs and feminizing hormones. A summary of the findings in the form of infographics will be made available to you. The study is of global importance for trans women with HIV, an underserved population, and their care providers.

Conflicts of Interest

The Principal Investigator (Dr. Mona Loutfy) is the Director of Research and President of Maple Leaf Research, the sponsor for this study. However, Dr. Mona Loufty will not participate in the consenting process.

Who do I call if I have questions?

- If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor in charge of the study at this institution.
- Dr. Mona Loutfy at Maple Leaf Research/Maple Leaf Medical Clinic:

  416-465-0756 then 1, or mona.loutfy@wchospital.ca
- You can also contact the Research Manager of Maple Leaf Research:
  - Roberta Halpenny at: roberta@mlmedical.com

    Main phone: 416-465-7936 (M-F 8 am to 4 pm)

    Emergency: 416-454-9148 (24-hour contact)

This study has been reviewed by Veritas Independent Review Board (IRB). If you have any questions about your rights as a research participant or the Investigator's responsibilities, you may contact the Manager of Veritas IRB 24 hours per day and 7 days per week at 514-337-0442 or toll-free at 1-866-384-4221. An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the subject's rights and welfare in mind. If you have any study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you need to speak to a person independent from the Investigator and the research staff, and/or if the Investigator and the research staff could not be reached.

- This study has also been reviewed by the Research Ethics Board (REB) at Women's College Hospital. The chair of the REB can be contacted at ethics@wchospital.ca.

- This study has also been reviewed by the Research Ethics Board (REB) at Unity Heath Toronto. The chair of the REB can be contacted at researchethics@unityhealth.to .

Drug-drug interaction study between bictegravir/emtricitabine/ tenofovir alafenamide and feminizing hormones in trans women living with HIV

By signing this form, I confirm that:

- This research study has been fully explained to me and all my questions answered to my satisfaction
- I understand the requirements of participating in this research study
- I have been informed of the risks if any, of participating in this research study
- I have been informed of the rights of research participants
- I have read each page of this form
- I have been given the opportunity to clarify anything that I do not understand, and there is nothing I have read that I do not understand
- I authorize access to my research study data as explained in this form
- I have agreed to participate in this study or agree to allow the person I am responsible for to participate in this study
- This informed consent document may be placed in my medical records

The study doctor has my permission to communicate with my doctor regarding my enrolment in the trial, my medical history and my study results:

☐ Yes ☐ No

Name of Provider (s) _____

Study Participant Consents to Repeat Month 2 Visit (if needed)

☐ **YES**. As explained in the Month 2 Visit Repeat section, I agree for study staff, to **repeat** the Month 2 Visit if needed.

☐ **NO**. As explained in the Month 2 Visit Repeat section, I do not agree for study staff, to **repeat** the Month 2 Visit if needed.

Future Studies:

I agree to be contacted for any future trans- women research studies.

☐ Yes ☐ No

_____	_____	_____
Name of Participant (print)	**Signature**	**Date**

Person Obtaining Consent

By signing this form, I confirm that:

- This study and its purpose have been explained to the participant named above
- All questions asked by the participant have been answered
- I will give a copy of this signed and dated document to the participant

_____ _____ _____

Staff Obtaining Consent Name & Title **Signature** **Date**

The following attestation must be provided if the participant is unable to read or requires an oral translation:

Was the participant assisted during the consent process? ☐**NO** ☐**YES**

If **YES**, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

_____ _____ _____

Print Name of Interpreter Signature Date

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to and has had any questions answered.

_____ _____ _____

Print Name of Witness Signature Date

_____

Relationship to Participant

14 College Street • Suite 403 • Toronto, ON • M5G1K2
T 416.465.7936 F 416.465.0502 • www.mlmedical.com

Communication:

Maple Leaf Research Inc. (MLR) may need to reach you for various purposes related to your visits and care. Telephone is the primary form of communication, however, visit confirmations and other study documents (i.e. copy of your signed consent, visit instructions) may be sent to your email.

For virtual visits, additional forms of communication are required.

1. Visits will take place over zoom.
2. Blood Requisitions and other study documents (i.e. copy of your electronically signed consent, visit instructions) are sent to your email.
3. Questionnaires are completed electronically through REDCAP, a program the study team uses to collect your data. You will receive a link and password by email.

Maple Leaf Research staff will, whenever possible, use reasonable means to protect the security and confidentiality of information sent and received using electronic communications. However, certain forms of electronic communication are not entirely secure and MLR staff cannot guarantee the security and confidentiality of electronic communications.

For the forms of communication that you are comfortable using, provide your preferences and contact information (email address, cell phone number, etc.) associated with those methods of communication.

☐ **NO,** I do not agree to communicate using methods described above.

☐ **YES,** I have read, understand, and agree with communicating using the communications described above.

Phone Number(s) MLR May Call You At:	**Can leave a detailed message:**
Cell:	☐ yes ☐ no
Home:	☐ yes ☐ no
Email (s):	

If you cannot be reached, please provide an alternative contact: ☐ NA

Alternative Persons name:

Alternative Persons number: