CLINICAL RESEARCH
DIVISION OF INFECTIOUS DISEASES
Department of Medicine

8440 – 112 St
Edmonton, Alberta, Canada T6G 2B7
Tel: 780-407-6945
Fax: 780-407-6454
After Hours Pager: 780-407-8822
(Hospital Switchboard)

PARTICIPANT INFORMATION AND CONSENT FORM

A Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Switching from a Regimen of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate to Bictegravir/ Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected Adults who are Virologically Suppressed

Supervising Study Doctor: Dr. Stephen Shafran

WHY AM I BEING ASKED TO BE IN THIS STUDY?

You have been asked to take part in a clinical research study for adults with HIV-1 infection who are taking the single tablet regimen (STR) efavirenz/emtricitabine/tenofovir disoproxil fumarate (Atripla® or generic equivalent) and have a suppressed HIV viral load. A clinical research study is a scientific way to find out more information about new treatments. This study will test an anti-HIV STR called bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF). Health Canada recently approved B/F/TAF for use by the general public. Although this new medication is approved it is not readily available because provincial funding is not yet available.

Before you make a decision one of the research assistants will go over this form with you. You are encouraged to ask questions if you feel anything needs to be made clearer. You will be given a signed and dated copy of this form for your records.

WHAT IS THE PURPOSE OF THIS STUDY?

Atripla (ATP: FTC/TDF/EFV) was the first single pill treatment for HIV and was the most prescribed first-line treatment from approximately 2008 to 2013 for people infected with HIV. However, ATP has not been recommended as a “preferred” treatment for HIV since 2015, due to there now being single pill treatments that work better. There are a lot of people who are still taking ATP and it is working for them. However, it has the potential to cause serious side effects (chronic kidney disease and fractures and serious neurological effects). These side effects are caused by components in ATP (namely the TDF and EFV parts). Also, the efavirenz (EFV) component is not compatible for treatment of Hepatitis C – which is often also seen in people who have HIV. For these reasons, there is a need to find a better alternative treatment for these people currently being treated with ATP.

B/F/TAF (bictegravir/FTC/TAF) is a single pill drug treatment drug that contains neither TDF nor EFV. This study is looking at whether changing people to this new drug treatment will continue to suppress their HIV and have fewer side effects.

It is thought that B/F/TAF will provide a potent, convenient, and well-tolerated regimen for the long-term treatment of patients with HIV infection and may show improvements in kidney function and bone density compared with Atripla®.

The safety and how well B/F/TAF is tolerated, will be determined by using physical exams, laboratory tests, and any symptoms or problems you might experience during the study.

WHAT WILL HAPPEN IN THE STUDY?

We are hoping to enroll 200 people in this study in Edmonton.
This is a randomized, double-blind, placebo-matched study. All participants will receive Health Canada approved therapy for their condition.

Double-blind means you, your study Doctor(s) and the research assistants will not know which study drugs you will be taking.

Placebo-to-match (or placebo) means one of the study pills you take will look exactly like the drug but will have no medicine in it.
Randomized means the study treatment you take will be chosen by chance (like flipping a coin).

People in the study will receive one of the two study treatments listed below:

Treatment Group 1: B/F/TAF + Placebo-to-match Atripla®. Each pill is taken once daily, (total of 2 tablets).

Treatment Group 2: Atripla® + Placebo-to-match B/F/TAF. Each pill is taken once daily, (total of 2 tablets).

You have an equal chance of being assigned to Treatment Group 1 or Treatment Group 2.

All study treatments must be taken once a day, at approximately the same time every day, with or without food. It is very important that you take your study treatment every day.

HOW LONG WILL YOU BE ON THE STUDY?

Taking part in the blinded treatment phase of this study will last for 52 weeks (one year). During this time, you will be assessed 7 times (at Day 1, Weeks 4, 12, 24, 36, 48 and 52). Each visit will take approximately one hour.

At week 52, you will be told whether you were receiving B/F/TAF or Atripla® during the 52 weeks of blinded therapy and be given the option of receiving B/F/TAF. B/F/TAF will be supplied to you free of charge by the study until the Alberta HIV Program covers it.

WHAT WILL I BE ASKED TO DO WHILE I AM IN THE STUDY?

Being in a study usually means you have to do things over and above what is required for standard of care, so this should be considered when you are deciding if you want to be in the study. In order to participate in this study you will need to agree to do the following:

- Take the two study pills every day (one active, one placebo)
- Be assessed by the study staff (either in-person or via telehealth) and do the required blood, urine and the two bone density tests.
- Not get pregnant or get someone pregnant.
- When your study doctor asks you about your health and medications you are taking now or start taking while in the study it will be important for you to give them complete information. Leaving information about your past health conditions and medication you are taking out can put your health at risk, especially in a study where we don't know all there is to know about a new drug.
- Concentration of study drug may decrease with antacids. You may not take antacids (e.g., Tums or Rolaids), the ulcer medication sucralfate, and vitamin or mineral

supplements that contain calcium, iron or zinc for a minimum of 6 hours before and 2 hours after any dose of study drug.
- You cannot take prescription drug therapy for osteoporosis (calcium and/or vitamin D is allowed)
- Bring back all unused study drugs and all study drug containers (even if they are empty or used). Your Study coordinator will discuss adherence and ask about any doses you did not take or if you took any extra doses.
- Talk to the study doctor before taking any new medications

For your safety. it is very important to follow all instructions given to you while you are taking part in this study. If you do not, you may no longer be able to take part in the study.

WHAT WILL HAPPEN AT EACH STUDY VISIT?

If you agree to take part in the study, you will have screening tests and procedures to determine if you meet the requirements to take part in this study. This screening visit takes place no more than 30 days before the study starts and will include the following tests:

- Blood samples will be collected at screening, weeks 4, 12, 24, 36 and 48. Blood testing will be done to measure HIV viral load as well as to monitor for safety.
- Urine samples will be collected at screening, week 24 and week 48.
- Measurement of bone density will be done twice using a machine called DXA: once between screening and day 1 and the second time around week 48.
- Quality of life questionnaire will be completed at screening and week 4.
- Dispense study medication and take back any unused medication from the last visit.
- Ask you about any updates to your health and any side effects you may have had since the last visit.

WHAT ARE THE POSSIBLE RISKS OF BEING IN THIS STUDY?

Like with taking any medicine, there are always side effects that are possible. The following section outlines the possible risks/side effects from being in this study:

Bictegravir/Emtricitabine/Tenofovir alafenamide (B/F/TAF)

The safety information known about the B/F/TAF tablet is from 3 studies in which 924 HIV-1 infected patients received B/F/TAF for 48 weeks. Diarrhea was the most frequent side event (11%), but this is about the same rate reported in the other anti-HIV regimens in the same 3 studies. Common side effects (seen in >5-10% of people) included headache, nausea, fatigue, joint pain, and back pain, at rates similar to what is reported with other anti-HIV regimens.

Switching From a Stable Regimen

You are currently taking a medication that is effectively treating your HIV infection. In this study if you are randomized to the group that gets the B/F/TAF tablet you will be changing from a stable regimen that is working to a potential new regimen. When switching from one antiviral regimen to another, there is a very small risk that the virus will not be controlled with the new regimen, that the virus could develop resistance to the medications, and that the new regimen could cause new side effects. To monitor you for this, viral load, possible resistance, and side effects will be frequently and carefully monitored during this study to minimize these risks. If you develop resistance to a drug for HIV, your doctor will make changes to your drug regimen

Blood Draws

Collecting a blood sample from a vein may cause pain, bruising, lightheadedness, fainting, and very rarely, infection at the site of the needle stick.

DXA
You will be exposed to a very small amount of radiation during each DXA scan performed for the study (less radiation than a chest X-ray). The risk from this amount of radiation has been categorized by the AHS Regional Radiation Safety Committee as 'negligible'. DXA scans are generally considered to be harmless.

Allergic Reaction
Allergic reaction is always possible with a drug you have not taken. Serious allergic reactions that can be life-threatening may occur. Some things that happen during any allergic reaction to any type of medication are:

- rash
- having a hard time breathing
- wheezing when you breathe
- sudden drop in blood pressure
- swelling around the mouth, throat, or eyes
- fast pulse
- sweating

Please seek treatment and alert the study doctor and study staff immediately if you have any of the above symptoms during the study.

Unknown/Unexpected Risks and Discomforts
There may be side effects that are not known or happen rarely when participants take these study drugs. You will be told of any new information that might cause you to change your mind about continuing to take part in this study as soon as the information is available.

PREGNANCY AND BREASTFEEDING
Please share this information with your partner if it is appropriate and we would be happy to discuss any of this with them.

The effects of B/F/TAF on a developing fetus (unborn baby) as well as on exposed infants are not known in humans. Any female able to become pregnant must have a negative pregnancy test to enroll. Females who are breastfeeding will not be enrolled in this study.

It is very important while you are in this study that you do not become pregnant if you are a female, or do not cause others to become pregnant if you are a male. Not having heterosexual sex is the only certain way to prevent pregnancy.

Men who have sex with female partners who are capable of becoming pregnant are required to use condoms from the first study drug dose, throughout the study.

If you cause your female sex partner to become pregnant while you are in the study the study drug may or may not harm an unborn baby. As the risk to your partner and unborn baby is not known, it is recommended for your partner to receive appropriate prenatal care.

If you are a woman who has sex with a male partner, you will be required to use effective methods of birth control from the screening visit, throughout the study and for 30 days following the last dose of study drug.

Acceptable methods of birth control include:

- Post-menopausal state
- Intrauterine hormone-releasing system (IUS)

- Intrauterine device (IUD)
- Tubal sterilization or hysterectomy
- Essure micro-insert system
- Vasectomy in male partner
- Barrier Methods
    - Female barriers: Diaphragm with spermicide or Cervical cap with spermicide
    - Male barriers: Male condom (with or without spermicide)
- Hormonal Methods
    - Oral contraceptives (either combined or progesterone only)
    - Injectable progesterone
    - Implants of levonorgestrel
    - Transdermal contraceptive patch
    - Contraceptive vaginal ring

If you are female and become pregnant or suspect that you have become pregnant while in the study and within 30 days of last dose of study drug, you will be required to stop taking all the study drugs and to notify your Study Doctor immediately. You will be discontinued from the study and provided with alternative antiviral therapy.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

We do not know if you will have any direct health benefits from being in this study. However, your participation may help other patients with HIV infection by learning more about B/F/TAF in patients who have previously received Atripla®.

WHAT ARE YOUR TREATMENT OPTIONS?

You do not have to participate in this study in order to receive antiviral treatment for HIV. Your Study Doctor will discuss appropriate treatment options and the risks and benefits with you.

DO I HAVE TO TAKE PART IN THIS STUDY?

Being in this study is your choice. If you decide to be in the study, you can change your mind and stop being in the study at any time, and it will in no way affect the care or treatment that you are entitled to.

CAN MY PARTICIPATION IN THE STUDY END EARLY?

Your participation in this study may be stopped for various reasons:
Your Study Doctor may decide to take you out of the study: for your medical safety, if your HIV is not responding to the treatment, if you are not following the study procedures, or if the approval for the study is withdrawn.

If you are taken off the study, you will no longer receive the study drug(s). If your study drug(s) is stopped, your Study Doctor will closely monitor your overall health and offer alternative treatment. When you leave the study, we will not collect new health information about you, but we will need to keep the data that we have already collected.

WHAT WILL IT COST ME TO PARTICIPATE?

The study drugs used in this study will be given to you free of charge. All study visits and fees for lab tests and procedures that are part of this study will be provided at no cost to you.

WILL I BE PAID TO BE IN THE STUDY?

For each completed visit, you may be reimbursed $20 per visit for your reasonable expenses related to this study, such as time, travel, parking, or meals.

If you discontinue early from the study, you will only receive reimbursement for the study visits you completed.

WHAT HAPPENS IF YOU ARE INJURED?

If you become ill or injured as a result of being in this study, you will receive necessary medical treatment, at no additional cost to you. By signing this consent form you are not releasing the investigator(s), and/or institution(s) from their legal and professional responsibilities.

WILL MY INFORMATION BE KEPT PRIVATE?

During the study we will be collecting health data about you. We will do everything we can to make sure that these data are kept private. No data relating to this study that includes your name will be released outside of the study doctor's office. The results of this study may be presented at meetings or in publications, however you will not be personally identified in any presentation or publication. Sometimes, by law, we may have to release your information with your name so we cannot guarantee absolute privacy. However, we will make every legal effort to make sure that your health information is kept private.

The study doctor/study staff may need to look at your personal health records held at the study doctor's office, and/or kept by other health care providers that you may have seen in the past (i.e. your family doctor). Any personal health information that we get from these records will be only what is needed for the study.

During research studies it is important that the data we get are accurate. For this reason your health data, including your name, may be looked at by people from the University of Alberta clinical auditors or members of their Research Ethics Board.

By signing this consent form you are giving permission for the study doctor/staff to collect, use and disclose information about you from your personal health records as described above. After the study is done, we will still need to securely store your health data that was collected as part of the study. At the University of Alberta, we keep data stored for 5 years after the end of the study.

WHAT IF I HAVE QUESTIONS?

If you have any questions about the research now or later, please contact the study staff at 780-407-6945 or the study doctor at 780-492-3319. In case of emergency after hours please call the hospital switch board at 780-407-8822 and have the adult infectious diseases physician paged.

If you have experienced a research related injury, please contact your Study Doctor or study staff.

If you have concerns about your rights as a study participant, you may contact the Research Ethics Office at (780) 492-2615. This office is independent of the study investigators.

The study is being funded by a grant from Gilead Sciences Inc. The Institution is getting money to cover the costs of doing this study.

A description of this clinical trial will be available on www.clinicaltrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CLINICAL RESEARCH
DIVISION OF INFECTIOUS DISEASES
Department of Medicine

8440 – 112 St
Edmonton, Alberta, Canada T6G 2B7
Tel: 780-407-6945
Fax: 780-407-6454
After Hours Pager: 780-407-8822
(Hospital Switchboard)

CONSENT

Title of Study: A Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Switching from a Regimen of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate to Bictegravir/ Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected Adults who are Virologically Suppressed

Principal Investigator: Dr. Stephen Shafran **780-492-3319 or 780-407-8822**

Study Coordinators: **780-407-6945**

Do you understand that you have been asked to be in a research study?	Yes ☐	No ☐
Have you read and received a copy of the attached Information Sheet?	Yes ☐	No ☐
Do you understand the benefits and risks involved in taking part in this research study?	Yes ☐	No ☐
Have you had an opportunity to ask questions and discuss this study?	Yes ☐	No ☐
Do you understand that you are free to leave the study at any time, without having to give a reason and without affecting your future medical care?	Yes ☐	No ☐
Has the issue of confidentiality been explained to you? Do you understand who will have access to your records including personally identifiable health information?	Yes ☐	No ☐
Do you want the investigators to inform your family doctor that you are participating in this research study?	Yes ☐	No ☐

If so, please provide your doctor's name: _____

This study was explained to me by: _____

I agree to take part in this study.

Research Participant:

_____	_____	_____
Signature	Printed Name	Date & Time

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

_____	_____	_____
Signature of Investigator or Designee	Printed Name	Date & Time