Partners HealthCare System
Research Consent Form

Subject Identification

General Template
Version Date: August 2016

Protocol Title: Effects of Bictegravir-Emtricitabine-Tenofovir Alafenamide on Coronary Flow Reserve in Stable HIV Patients (B/F/TAF-CFR) - Pilot Study

Principal Investigator: Marcelo Di Carli, MD

Site Principal Investigator: Virginia Triant, MD

Description of Subject Population: Patients with Stable HIV

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. 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.

Why is this research study being done?

We are doing this research study to find out if the drug called Biktarvy (Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF)) can help improve the blood flow to the heart in people with HIV. We think this is because Biktarvy reduces the inflammation in the heart arteries.

Biktarvy is approved by the U.S. Food and Drug Administration (FDA) for treatment of HIV. BIKTARVY contains the medicines bictegravir, emtricitabine, and tenofovir alafenamide.

This research study will compare the blood flow to your heart before starting Biktarvy and after 24 weeks of taking the drug. Biktarvy comes in tablet form and you will take it by mouth once a day.

The gold standard for measuring blood flow to the heart with imaging is known as Positron Emission Tomography (PET). A PET scan is a test that uses a radioactive tracer (dye) called N13 Ammonia. PET scans allow doctors to see the blood flow to the muscle of the heart. It also lets us calculate the blood flow using a measure called Coronary Flow Reserve (CFR). CFR adds information to help doctors diagnose heart disease. The use of N13 for PET scans is FDA-approved and these scans are routinely performed at Brigham and Women's Hospital.

We are asking you to take part in this study because you have HIV and are currently taking abacavir/lamivudine/dolutegravir (Triumeq). As part of your participation in this study, we will ask you to stop taking Triumeq for 24 weeks. During this time, you will take Biktarvy, which will be provided by the study. We believe that imaging studies such as PET will help doctors see if the Biktarvy has less effects on the heart than other HIV treatments.

About 30 subjects will take part in this study. Subjects will be recruited from Brigham and Women's Hospital as well as Massachusetts General Hospital, Tufts Medical Center, and Boston Medical Center. All research activities will be done at Brigham and Women's Hospital.

Gilead Sciences, Inc. is paying for this research to be done.

How long will I take part in this research study?

It will take you about 6 months to complete this research study. During this time, we will ask you to make up to 4 study visits to the Brigham and Women's Hospital. We will also call you 3 times to remind you of your visits and see how you are feeling.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Any woman who is seeking to become pregnant or suspects she may be pregnant will not be enrolled in the study. We will draw a blood sample to test for pregnancy at the screening visit and before each administration of radiopharmaceutical in this study, if you are a woman able to become pregnant.

Screening Visit (up to 4 weeks before the baseline visit)

The screening visit will take about 1 hour. During this visit, we will do some tests and procedures to see if you qualify for the study. The study doctor will review the results of these tests and procedures. At this visit we will:

- Ask you questions about yourself to make sure you qualify for the study
- Check your "vital signs" (blood pressure and heart rate, and oxygen saturation). Oxygen saturation is how much oxygen is in your blood. It is measured by a small device that is placed on your finger.
- Let the study team know whether you have had any food for 4 hours prior to this visit.
- Draw blood from you for testing. The blood test will include a pregnancy test if you are a woman who is able to become pregnant. Pregnant and breast-feeding women cannot take part in this study. We will also draw blood to make sure you do not have hepatitis B. We will draw a total of about 26mL (approximately 5 teaspoons) of blood at this visit for clinical purposes. If you have already had any of these tests done within the past year, we will use those results.
- Possibly collect urine for a drug screen, which will test for the presence of recreational drugs. The test results will be available to the study investigator and may be available to your doctor. The results will not be entered in to your medical record, though positive results will disqualify you from participation.

Baseline Visit (Day 0)

This visit will take about 4 hours and will happen at the PET Imaging Center at BWH. At this visit, we will:

- Make sure that there have been no changes to your health since the screening visit.
- Ask you about your medical history and any current medications you are taking.
- Give you a physical exam, including height, weight and "vital signs" (blood pressure and heart rate, and oxygen saturation). Oxygen saturation is how much oxygen is in your blood. It is measured by a small device that is placed on your finger.
- Do a 12-lead electrocardiogram (ECG). An ECG is a test that checks the electrical activity of your heart. We will place several small, sticky pads on your chest, arms, and legs. Each pad has a wire attached. The wires connect to a machine that makes a recording of your heart rhythm. This painless test takes about 15 minutes.

- Draw blood from you for testing. The blood test will include a pregnancy test if you are a woman who is able to become pregnant. Pregnant and breast-feeding women cannot take part in this study. We will draw a total of about 9mL (approximately 2 teaspoons) of blood at this visit for clinical purposes and 29mL for research purposes if you agree, for a total of 38mL (approximately 8 teaspoons) at this visit.

- Perform PET/CT scan

PET/CT scan:

- You must not have caffeine within 12 hours prior to this test and you must also not eat any food for 4 hours prior to this visit.

- You will be instructed to not take your beta blockers, calcium channel blockers and arterial vasodilators for 24 hours prior to the PET scan. We will help you identify any medications that fit one of these categories.

- We will place an intravenous (IV) catheter, which is a thin, flexible plastic tube.

- Adhesive patches will be placed on your chest to monitor your heart during the test.

- You will be positioned in the PET/CT scanner. You will lie on a table and will be moved through the circular opening of the donut shaped PET/CT scanner. The table will move forward and backward as the scan is done. You will be asked to keep still during the scan. We will inject you with the radioactive tracer through the IV to take pictures of your heart at rest. These pictures take about 20 minutes.

- We will take you out of the scanner and you will have about a 20-minute break.

- You will be repositioned in the PET/CT camera again. One of the doctors will give you a medication to dilate the vessels in the heart. This injection will also be given through the IV. You will then be injected with a second dose of the radioactive tracer to take pictures of your heart at stress. These pictures will also take about 20 minutes.

Before you leave the hospital, we will provide you with enough study drug to last you until your next visit (Study Visit, Day 45).

How to take the study drug:

1. The study drug comes in the form of a tablet. You will take one (1) tablet a day.

2. Please take note of the potential side effects of the study drug as listed on page 8. Immediately contact study investigators or staff by email and/or phone for any of these symptoms or any other new or concerning symptoms.
3. Take the study drug by mouth, with or without food.
4. Swallow the study drug tablet whole. Do not crush, break, or chew the study drug tablets before swallowing.
5. If you miss a dose of the study drug, wait to take the next dose of the study drug at your regular time. Do not make up for the missed dose. Record the date and the dose you miss on the medication diary provided by study staff.
6. Do not take more than 1 dose at a time.
7. If you take too much the study drug, call your doctor, or go to the nearest emergency room right away.

We will give you a diary to record your daily intake of the study medication.

Day 14 (Telephone follow-up call 1)

This call will take less than 5 minutes.

During this phone call we will:

- Ask if you have made any changes to the medications you are taking.
- Remind you to immediately contact study investigators or staff by email and/or phone for any of the symptoms list on page 8 or any other new or concerning symptoms.
- Remind you to record your daily intake of the study medication on the diary.

Day 45 (study visit)

This visit will take about 2 hours and will happen at the PET Imaging Center at BWH. At this visit, we will:

- Ask you if you have been taking study drug as instructed by the study doctor. The study doctor or a member of the study staff will do a pill count from your drug bottle.
- Ask you if you have experienced any side effects listed in this consent form.
- Ask you about your medical history and any current medications you are taking.
- Give you a physical exam, including height, weight and "vital signs" (blood pressure and heart rate, and oxygen saturation). Oxygen saturation is how much oxygen is in your blood. It is measured by a small device that is placed on your finger.
- Confirm that you have not had any food for 4 hours prior to this visit.

- Draw blood from you for testing. We will draw a total of about 22mL of blood (approximately 4 teaspoons) at this visit for clinical purposes.
- Before you leave the hospital, we will provide you with enough study drug to last you until your next visit (Study Visit, Day 168).

We will give you a diary to record your daily intake of the study medication.

Day 126 (Telephone follow-up call 2)

This call will take less than 5 minutes.

During this phone call we will:

- Ask if you have made any changes to the medications you are taking.
- Remind you to immediately contact study investigators or staff by email and/or phone for any of the symptoms list on page 8 or any other new or concerning symptoms.
- Remind you to record your daily intake of the study medication on the diary.

Day 168 (End of Treatment)

This visit will take about 4 hours and will happen at the PET Imaging Center at BWH. At this visit, we will:

- Make sure that there have been no changes to your health since the Day 45 visit.
- Ask you if you have been taking study drug as instructed by the study doctor. The study doctor or a member of the study staff will do a pill count from your drug bottle.
- Ask you if you have experienced any side effects listed in this consent form.
- Collect the diary
- Ask you about your medical history and any current medications you are taking.
- Give you a physical exam, including height, weight and "vital signs" (blood pressure and heart rate, and oxygen saturation). Oxygen saturation is how much oxygen is in your blood. It is measured by a small device that is placed on your finger.
- Do a 12-lead electrocardiogram (ECG). An ECG is a test that checks the electrical activity of your heart. We will place several small, sticky pads on your chest, arms, and legs. Each pad has a wire attached. The wires connect to a machine that makes a recording of your heart rhythm. This painless test takes about 15 minutes.
- Draw blood from you for testing. The blood test will include a pregnancy test if you are a woman who is able to become pregnant. Pregnant and breast-feeding women cannot take part in this study. We will draw a total of about 26mL of blood (approximately 5 teaspoons) at this visit for clinical purposes and 29mL (approximately 3 teaspoons) for

research purposes if you agree, for a total of 55mL (approximately 8 teaspoons) at this visit.

- Perform PET/CT scan

PET/CT scan:

- You must not have caffeine within 12 hours prior to this test and you must also not eat any food for 4 hours prior to this visit.
- You will be instructed to not take your beta blockers, calcium channel blockers and arterial vasodilators for 24 hours prior to the PET scan. We will help you identify any medications that fit one of these categories.
- We will place an intravenous (IV) catheter, which is a thin, flexible plastic tube.
- Adhesive patches will be placed on your chest to monitor your heart during the test.
- You will be positioned in the PET/CT scanner. You will lie on a table and will be moved through the circular opening of the donut shaped PET/CT scanner. The table will move forward and backward as the scan is done. You will be asked to keep still during the scan. We will inject you with the radioactive tracer through the IV to take pictures of your heart at rest. These pictures take about 20 minutes.
- We will take you out of the scanner and you will have about a 20-minute break.
- You will be repositioned in the PET/CT camera again. One of the doctors will give you a medication to dilate the vessels in the heart. This injection will also be given through the IV. You will then be injected with a second dose of the radioactive tracer to take pictures of your heart at stress. These pictures will also take about 20 minutes.

Day 174 (Telephone follow-up call 3)

This call will take less than 5 minutes. We will call you by telephone at about 1 week (5 to 7 days) after your last visit to see how you are feeling.

What are the risks and possible discomforts from being in this research study?

^{13}N-Ammonia PET/CT Scan:

As a result of your participation in this study you will be exposed to radiation from Nuclear Medicine scans of your heart. Please note that this radiation is not necessary for your medical care and is for research purposes only. The radiation you will receive from participation in this study is estimated to be 6 milliSieverts (mSv). A mSv is a unit of radiation dose. For comparison, everyone receives radiation exposure from natural background sources from the earth and the sky. The dose that you receive from participation in this research study is about the same as you would normally receive in 2 years from these natural sources.

Scientists disagree on whether radiation doses at these levels pose significant health risks. A possible effect that could occur at doses associated with this study is a slight increase in the risk of developing cancer later in life.

If you have taken part in other research studies in the past 12 months that include tests with radiation, please tell us before you enroll in the study. If your past radiation exposure is more than our current guidelines allow, you may not be able to take part in this study. If you take part in a similar study involving radioactivity in the next 12 months, you should tell the doctor ordering the scans that you took part in this study.

Please indicate below if you have taken part in research studies that have involved radiation exposure.

___ YES, I have taken part in research studies that have involved radiation exposure within the last 12 months.

INITIALS: _____

___ NO, I have not taken part in research studies that have involved radiation exposure within the last 12 months.

INITIALS: _____

Biktarvy:

Biktarvy, the study drug for this research study, is FDA-approved and is prescribed for the treatment of HIV.

Very common side effects (more than 10 in 100):

- Diarrhea
- Headache

Common side effects (between 1 and 10 in 100):

- Nausea
- Vomiting
- Stomach pain
- Indigestion
- Passing gas
- Tiredness
- Rash

If you are infected with hepatitis B virus (HBV), there is a possibility of an unexpected worsening of hepatitis B if you stop taking Biktarvy.

Do not take the following medications while you are in the study. Taking these drugs and Biktarvy together may cause serious side effects:

- Dofetilide
- Rifampin
- Any other medicines to treat HIV

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements, antacids, laxatives, or vitamins

Pregnancy:

Radiation may cause physical or genetic damage to a fetus, so you should not participate in this study if there is a chance you may be pregnant or if you are breastfeeding.

Regadenoson:

Regadenoson stress as performed in this study has been used routinely for many years for evaluating patients with known or suspected CAD. It is FDA approved. The most common side effects associated with the regadenoson bolus include:

Very common – more than 1 out of 10:

- Flushing
- Shortness of breath

Common – between 1 and 10 out of 100:

- Chest pain/pressure
- Palpitations
- Headache
- Mild low blood pressure

Uncommon - between 1 and 10 out of 1,000:

- Heart block

Adenosine:

As part of the PET scan, you will receive a medicine called adenosine if you have a history of seizures. The side effects associated with adenosine include:

Very common – more than 1 out of 10:

- Facial flushing
- Shortness of breath/dyspnea
- Head pressure

Common – between 1 and 10 out of 100:

- Headache
- Palpitations
- Chest pain
- Chest pressure
- Hyperventilation
- Nausea

Uncommon - between 1 and 10 out of 1,000:

- Sweating
- Hypotension
- Lightheadedness/ dizziness
- Tingling in arms
- Numbness
- Apprehension
- Blurred vision
- Burning sensation
- Heaviness in arms
- Neck and back pain
- Metallic taste

Aminophyline:

The study doctor may determine it is necessary to give you aminophyline if the regadenoson makes it harder for you to breath. Aminophyline is FDA-approved to treat shortness of breath and other symptoms associated with breathing difficulties. The most common side effects associated with aminophyline include:

Uncommon - between 1 and 10 out of 1,000:

- Nausea
- Vomiting
- Headache
- Insomnia
- High heart rate

Blood Draws and Intravenous Catheter Risks

You may have pain, bleeding, bruising, or infection at the place where we take blood samples or where we place the IV catheter. In the rare case that you develop a reaction, we will treat it immediately.

We would like to store some of your samples and health information for future research related to heart disease and HIV. We will label your samples and health information with a code instead of your name. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password protected database.

> Do you agree to let us store your samples and health information for future research related to heart disease and HIV?
>
> ☐ Yes ☐ No Initials_____

If later you change your mind and want your samples destroyed, contact the study doctor.

Unknown Risks:

There may be additional risks that are not known yet.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this research study. However, we believe that Biktarvy will have less side effects than abacavir/lamivudine/dolutegravir.

Information learned from this study may help doctors diagnose heart disease in patients with HIV more accurately.

What other treatments or procedures are available for my condition?

Your Study Doctor will discuss appropriate treatment options and the risks and benefits with you.

You can discuss if you want to have any treatment or if you want to choose other antiretroviral medications (ARVs) to treat your disease, which may include those that are already approved and sold.

Instead of being in this study you have the choice of:

- Treatment with other prescription drugs available to you such as Triumeq, (Abacavir/lamivudine, dolutegravir), Prezcobix (Darunavir/Cobicistat), Edurant (Rilpivirine), Raltegravir, Genvoya (Elvitegravir/cobicistat/tenofovir/emtricitabine).
- Treatment with experimental drugs, if you qualify
- No treatment

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will I be paid to take part in this research study?

We will pay you up to $500 including meals and parking vouchers if you complete the study. If you do not complete the study, we will pay you as follows:

Screening Visit:	$50
Baseline Visit:	$200
Day 45 Visit:	$50
End of Treatment Visit:	$200
TOTAL	$500

We will also give you a 6 to 24-hour parking voucher for all visits.

What will I have to pay for if I take part in this research study?

Study funds will cover the cost of all research-related study visits and for all procedures done for study purposes only.

Although study funds will pay for certain study-related items and services, we may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care.

If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Marcelo Di Carli, MD is the person in charge of this research study. You can call him at **617-732-6291 M-F 9-5.** You can call Dr. Di Carli 24-hours a day/7 days a week by calling the BWH page operator at 617-732-5656 and asking to page Dr. Di Carli at pager #32505.

If you have questions about the scheduling of appointments or study visits, call Laurel Campbell at 617-732-4237.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject

- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)

- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter	Date	Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name	Date	Time (optional)

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