Bictegravir/emtricitabine/tenofovir alafenamide plus doravirine in highly treatment-experienced men with multidrug-resistant HIV

NCT04538040
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INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Quest Clinical Research / "An open label study evaluating the safety and efficacy of switching from rilpivirine/emtricitabine/tenofovir alafenamide in combination with dolutegravir, to bictegravir/emtricitabine/tenofovir alafenamide in combination with doravirine, in male HIV+ subjects > 45 years with multi-drug resistant virus and virologic suppression (documented with at least one viral load result < 50 copies per mL) during the last 6 months on current therapy"**
Protocol Number:	**BETD-001**
Principal Investigator: (Study Doctor)	**F. Lisa Sterman, M.D., M.P.H.**
Telephone:	**415-353-0800** **415-863-3366 (24 Hour)**
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INTRODUCTION

You are invited to take part in a Phase IV research study. This study is studying the effect of switching your current HIV treatment from the combination of rilpivirine/emtricitabine/tenofovir alafenamide (ODEFSEY) in combination with dolutegravir (TIVICAY) to bictegravir/emtricitabine/tenofovir alafenamide (BIKTARVY) and Doravirine (PIFELTRO).

These medications are approved by the FDA for treatment of HIV and are used in combination with other HIV-1 medicines to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults.

Quest Clinical Research is sponsoring this research study.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

You must be honest with the study doctor about your health history or it may not be safe for you to be in this study.

BACKGROUND AND PURPOSE

You are being asked to participate in this study because you are a male, 45 years or older and have been diagnosed with HIV and receiving a combination of antiretroviral treatment (rilpivirine/emtricitabine/tenofovir alafenamide (ODEFSEY) in combination with dolutegravir (TIVICAY)) for more than 12 months. Antiretroviral drugs prevent HIV from inserting its genetic code into the DNA of an infected cell. They do this by blocking enzymes that HIV needs to hijack the host's DNA. HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

The new combination of study drugs should maintain the HIV virologic suppression and is designed with the goal of not being inferior to your current medication combination. It is not anticipated that this switch will place you at a greater risk than your current therapy.

The purpose of this research study is to:

- Test the safety and effectiveness of the combination drug
- Monitor for any improvement in well-being, weight changes and sleep pattern

About 30 subjects will participate in this study including 10 subjects who will participate in the PK portion (evaluation of the amount of drug in the body) of the study.

WHAT WILL HAPPEN DURING THE STUDY

Your participation in this study will last approximately 48 weeks and will include approximately 6 study visits to the study center. You may be asked to return to the clinic for an unscheduled visit to complete or retest a PK evaluation after completing the 6 study visits.

Screening/Baseline:

Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document.

- Obtaining informed consent for participation in the study
- Review of your demographic (personal) information such as date of birth, sex, ethnicity, race, and year of HIV diagnosis
- A physical examination including height, weight and BMI (body mass index)
- Your quality and pattern of sleep will be measured
- You will be asked to complete a questionnaire to check the effect of your health problems on your ability to work and perform regular activities
- Check your HIV virus count
- Check your CD4 count (less than 3 months of study entry)
- Your vital signs (temperature, respiratory rate, resting pulse and blood pressure) will be measured
- Collection of blood for safety lab tests
- Collection of a urine sample for routine lab tests
- You will be asked if you have had any recent illnesses or changes in your condition
- Inclusion and exclusion criteria will be reviewed to see if you qualify for the study
- If you qualify for the study, you will start taking your new drug regimen

Study Treatment:

You will have the following study visits and undergo the following procedures:

Visit 2 (Month 1 (give or take 14 days))

- Your blood may be collected to measure the amount of study drug in your blood if you participate in the PK portion of the study
- You will be asked if you have had any recent illnesses or changes in your condition
- A physical examination
- Your weight & vital signs (temperature, respiratory rate, and resting pulse and blood pressure) will be measured
- Collection of blood for safety lab tests
- Check your HIV virus count
- Collection of a urine sample for routine lab tests

Visit 3 (Week 12 (give or take 14 days)), Visit 4 (Week 24 (give or take 14 days)), Visit 5 (Week 36 (give or take 14 days))

- A physical examination
- Your weight & vital signs (temperature, respiratory rate, and resting pulse and blood pressure) will be measured
- Collection of blood for safety lab tests
- Check your HIV virus count
- Collection of a urine sample for routine lab tests
- You will be asked if you have had any recent illnesses or changes in your condition

Visit 6 (End of Study, Week 48 (give or take 14 days))

- A physical examination including weight and BMI
- Your quality and pattern of sleep will be measured
- You will be asked to complete a questionnaire to check the effect of your health problems on your ability to work and perform regular activities
- Your vital signs (temperature, respiratory rate, and resting pulse and blood pressure) will be measured
- Collection of blood for safety lab tests
- Check your HIV virus count
- Check your CD4 count
- Collection of a urine sample for routine lab tests
- You will be asked if you have had any recent illnesses or changes in your condition

PK Test/Retest

- You will be asked to take your study drug in the morning on the day before the PK sampling and record the time it was taken so you can let your study coordinator know
- On the day of PK sampling, you should not take your study drug until after you come to the clinic and your blood is drawn.
- Your blood will be collected to measure the amount of study drug in your blood at the following time points (in hours): -0.5, 0.5, 1, 2, 4, 6, 8, 12, & 24
- You will be asked to wait to take the study drug until after your blood has been drawn at the clinic on your hour 24 blood draw (the day after the PK sampling)

EXPECTATIONS

If you participate in this study, you will be expected to:

- Attend each visit at the study center
- Follow the instructions given by the study doctor
- Have all procedures done to you
- Notify the study doctor if you experience any health problems or illnesses during the study

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

You must tell the investigator or study staff about all side effects that you have. If you are not honest about your side effects, you may harm yourself by staying in this study.

If you don't understand what any of these side effects mean, please ask the investigator or study staff to explain these terms to you.

The study drugs can cause serious, life-threatening side effects. These include a buildup of lactic acid in the blood (lactic acidosis) and severe liver problems.

For bictegravir/emtricitabine/tenofovir alafenamide (BIKTARVY):

Possible

- Change in your immune system
- Kidney problems including kidney failure
- Too much lactic acid in the blood
- Severe liver problems
- Worsening of Hepatitis B virus infection
- Diarrhea
- Nausea
- Headache
- Tiredness
- Abnormal dreams
- Dizziness
- Insomnia

For Doravirine (PIFELTRO):

Possible

- Nausea
- Dizziness
- Headache
- Tiredness
- Diarrhea
- Stomach pain
- Abnormal dreams
- Rash
- Insomnia
- Altered state of consciousness

When you take more than one drug at a time, the side effects can be worse or different than if you take either drug by itself.

Until you know how the drug(s) will affect you, you should use caution by avoiding stairs, not driving a car or working with machinery.

RISKS OF STUDY PROCEDURES

- Blood samples: Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.
- Questionnaires: The questionnaires used in this study may be upsetting. You do not need to answer any questions that you are not comfortable with.

Blood Samples

Blood samples will be taken by single needle-sticks or by a tube that is left in your arm. You cannot choose how the blood is taken.

There will be about 9 time points during the PK collection. The total amount of blood drawn will be about 36 ml. For comparison, the standard blood donation is about 480 mL (two cups).

UNFORESEEN RISKS

There may be other risks for the study drugs, especially when given in combination with each other, that are unknown at this time. Additionally, there may be unknown risks to a pregnancy, embryo, or fetus if your female partner becomes pregnant.

ALTERNATIVES TO PARTICIPATION

You do not have to be in this study to receive treatment for your HIV. Your options may include continuing your current therapy or standard of care.

Please talk to the study doctor about your options before you decide whether or not you will take part in this study.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

BENEFITS

You may benefit as a result of your participation in this study. There is, however, no guarantee that you will benefit from your participation in this study. Information learned from the study may help other people in the future. You may maintain your weight and you may maintain your quality of life or may have improvement in your quality of life.

COMPENSATION FOR PARTICIPATION

You will be paid up to a total of $300.00 if you complete this study or $550.00 if you also participate in the intensive PK evaluation. You will be paid for the visits you complete according to the following schedule:

$50.00 for Visits Screening/Baseline, Month 1, 3, 6, 9, 12.
$300.00 for Visit Month 1 if you participate in PK evaluation.
$300.00 for PK evaluations performed after Month 1.

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid after each visit.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The Investigator, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and other state or federal regulatory agencies and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

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.

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. Please be aware that some insurance plans may not pay for research-related injuries. You should contact your insurance company for more information. You will not lose any of your legal rights or release the sponsor, the Investigator, the study staff, or study site from liability for mistakes by signing this consent document.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

COSTS

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you. Most of you will obtain your drugs through insurance, but we may be able to provide the drugs for you if insurance does not cover the cost.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00052105.

CONSENT FOR OPTIONAL SUB-STUDY

You are also being asked to participate in an optional sub-study to measure the amount of study drug in your blood.

You may decide not to participate in the optional sub-study. If you decide not to participate in the sub-study, your decision will have no impact on your ability to participate in the main study and will have no impact on any other benefits to which you would otherwise be entitled.

Please indicate your preference below:

❒**YES** _____ (initials) I agree to participate in the sub-study described above.

❒**NO** _____ (initials) I do not agree to participate in the sub-study described above.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

If you leave the study for any reason, the study doctor may ask you to come back for a follow-up visit 90 days after you discontinue treatment to have some end-of-study tests for your safety.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the Investigator may ask you to have some end-of-study tests for your safety.

PRIMARY HEALTH CARE PROVIDER NOTIFICATION OPTION

I consent to having my family doctor or primary health care provider notified by the study site of my participation in this study and/or any significant findings related to my health (please check yes or no).

❒**YES** (If yes, please complete the information below)

❒**NO**

Name and address of family doctor or primary health care provider:	Name:
	Address:
Telephone and Fax Number:	Tel:
	Fax:

SUBJECT'S BILL OF RIGHTS

If you have not already been given a separate copy of the California Experimental Research Subject's Bill of Rights, you will be given one at your visit. If you have not received a copy of this document, please notify study staff.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed and dated consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and research team will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the research team may share health data about you with authorized users. Authorized users may include

- Representatives of Quest Clinical Research.
- Representatives of DP Clinical Inc.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this research, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the drug combination works and is safe and effective
- To compare the drug combination to rilpivirine/emtricitabine/tenofovir alafenamide (RPF/FTC/TAF) in combination with dolutegravir.
- For other research activities related to the bictegravir/emtricitabine/tenofovir alafenamide in combination with doravirine.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date