Johns Hopkins University

Bioequivalence of Crushed and Whole Genvoya Tablets
(Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fumarate)

NCT03717129

5-21-2019

If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Analysis of Crushed and Whole Genvoya (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) Tablets**

Application No.: **IRB00110315**

Sponsor: **Gilead Sciences**

Principal Investigator: **Craig Hendrix, MD**
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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.

- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

This research is being done to see whether whole and crushed/dissolved Genvoya tablets are comparable in terms of how they are absorbed, distributed and excreted by the body.

Genvoya is a combination of four antiretroviral medications, medications that target types of viruses, in one tablet. It is approved in the United States by the Food and Drug Administration (FDA) to be taken daily for the treatment of HIV infection. The four antiretroviral medications included in the Genvoya tablet are: elvitegravir, emtricitabine, cobicistat, and tenofovir alafenamide.

Many HIV-infected patients have difficulty swallowing whole tablets of antiretroviral medications such as Genvoya. Therefore, it is important to find out whether crushing tablets such as Genvoya, to make it easier for patients to swallow, affects the effectiveness of its antiretroviral medications and potentially their effect to control HIV infection.

Healthy HIV negative adult men and women, without active hepatitis B may join this study. Since participants will only be given two doses of Genvoya in this study, individuals with hepatitis B and/or HIV will not be allowed to participate, because they require daily doses of medications for their lifetime to treat these infections. In addition, certain commonly prescribed medications can affect and/or may be affected by Genvoya. Therefore, only healthy adult subjects not taking medications prohibited in this study will be allowed to participate.

Women who screen for the study must not be pregnant or breastfeeding and must use a reliable form of contraception for the duration of the study.

How many people will be in this study?

Up to 20 individuals may be enrolled in the study to assure that 12 healthy men and women adult volunteers will be complete the study.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

Screening Visit:

This study has one screening visit that will take about 1 - 2 hours. The purpose of the screening visit is to confirm if it is safe for you to join the study. The screening visit will take place at the Johns Hopkins Drug Development Unit (DDU). The following will take place at the screening visit.

- You will be asked to sign this form after you have reviewed it carefully and had the chance to ask questions about the study.
- You will have a little less than 2 tablespoons of blood collected for the following:
    - An HIV test. You may be asked to sign a separate State of Maryland consent form for this HIV test. This test must be negative for you to be in the study. If the HIV test is positive it does not always mean you are infected with HIV. It does mean you will need further testing and you will receive counseling about this issue.

- Hepatitis B antigen. If you have a positive hepatitis B antigen it means that you have active hepatitis B virus. This test must be negative for you to be in the study. If you have a positive hepatitis B antigen you will be referred back to your primary care clinician for further evaluation.
  * The law requires us to report positive HIV and Hepatitis B tests to the health department. This reporting will include information that identifies you (for example name, date of birth, home address, phone number, etc.) as required by Maryland law. The health department may use this information to contact you for further follow up and/or to help conduct health surveillance activities aimed at preventing or controlling diseases.
- Blood tests to make sure you do not have other medical problems such as kidney and/or liver disease, or anemia.

- You will be asked questions about your medical and medication history.
- You will have a physical examination by a study clinician.
- If you are a woman, you will have a urine pregnancy test performed to see if you are pregnant. The test must be negative for you to participate in the study.
- You will be advised to use the recommended birth control method.

Whole Tablet Period: (Administration of Single Dose of Genvoya Whole Tablet) – 4 study visits on Days 1, 2, 3 and 4

- If you pass the screening visit you will return for the entry visit (Day 1).
- All study visits will take place in the Drug Development Unit.
- The Day 1 Visit will last about 14 hours. The Day 2, 3 and 4 visits will last about 30 minutes.
- The purpose of the entry visit is to give you a single dose of Genvoya whole tablet at the research unit and start the blood collections to measure all four antiretroviral medications in Genvoya.
- If you have any new medical problems since your last visit, you will be examined by a study clinician at these visits.
- You will be provided with meals at the Day 1 Visit.
- At the Day 1 Visit, you will also have a small intravenous (IV) catheter inserted into your arm or hand so that we may draw blood without sticking you repeatedly. We will draw blood from the catheter 13 times over the next 14 hours to measure the medications in Genvoya in your blood and assess your kidney function. The total amount of blood that will be collected on Day 1 will be about 7 tablespoons. The catheter will be removed at the end of the visit. If you are a women, you will have a urine pregnancy test prior to taking the Genvoya. This test must be negative for you to continue in the study.
- You will return to the clinic the following day (Day 2) to have about 2 teaspoons of blood drawn, about 24 hours after taking Genvoya. The study team will again ask you questions about your health and if you have any new medical problems, you may be examined by a study clinician.
- You will return to the clinic the following day (Day 3) to have about 2 teaspoons of blood drawn, about 48 hours after taking Genvoya. The study team will again ask you questions about your health and if you have any new medical problems, you may be examined by a study clinician.
- You will again return to the clinic the following day (Day 4) to have about 2 teaspoons of blood drawn about 72 hours after taking the Genvoya medication. The study team will again ask you questions about your health and if you have any new medical problems, you may be examined by a study clinician.

You will return 7 days after taking the Genvoya tablet, for the First Safety Visit – see below.

First Safety Visit

After completing all evaluations for the Whole Tablet Period, and 7 days after taking the whole tablet, you will be asked to return to the research unit your first safety visit, to monitor your health during the study. During this visit, we will collect about 2 teaspoons of blood to check a number of tests, including those to monitor your kidney and liver function, to make sure that Genvoya is not causing any problems. If your blood work shows abnormal results that require further action, you will be contacted with additional instructions that could require additional evaluations. If all your evaluations are considered normal, you will be instructed to return to the research unit 7 days later for your next study visits.

Crushed/Dissolved Tablet Period (Administration of Single Dose of Genvoya Crushed/Dissolved Tablet) - 4 study visits on Days 1, 2, 3 and 4

After you complete your first study safety visit, and a minimum of 14 days after taking the whole tablet of Genvoya, you will be asked to return for of the Crushed/Dissolved Tablet Period. Genvoya will be given to you during this period as a crushed/dissolved tablet mixed with water. You will return to the clinic to complete the same blood collections as in the Whole Tablet Period, to measure the four antiretroviral medications in Genvoya in your blood (see Whole Tablet Period above).

After completing all the blood collection for this period ,you will be instruct to return 7 days later for your final safety and study visit (see below).

Final Safety Visit/Final Study Visit

After completing all evaluations for the Crushed/Dissolved Tablet Period, and 7 days after taking the crushed/dissolved tablet, you will be asked to return to the research unit your final safety/study visit. During this visit, we will collect about 2 teaspoons of blood to check a number of tests, including those to monitor your kidney and liver function, to make sure that Genvoya is not causing any problems. If your blood work shows abnormal results that require further action, you will be contacted with additional instructions that could require additional evaluations. If all your evaluations are considered normal, you will be finished with study participation.

How long will you be in the study?

You will be in this study for about 5 weeks.

Future Contact:

We would like your permission to contact you about other studies you may be eligible for in the future. Please indicate your choice below about being contacted for future research.

□ YES _____ _____
Signature of Participant Date

□ NO _____ _____
Signature of Participant Date

Request to Collect and Store Biospecimens for Future Research:

As part of this research study, we would like to ask you to let us store your biospecimens and health information for future research. This research could include other diseases.

If you consent to allow us to store your biospecimens for future research and then later change your mind, you can withdraw your consent and your biospecimens will be destroyed.

The study doctor can provide you with additional information if you have questions. In addition, further information about our use of your biospecimens can be found in this consent document under the heading "*What happens to Data and Biospecimens that are collected in the study?"*

□ YES _____ _____
Signature of Participant Date

□ NO _____ _____
Signature of Participant Date

4. What are the risks or discomforts of the study?

Risks of Study Procedures:

Blood Draw: The risks and discomforts of blood drawing are slight. The vein may be damaged by the needle and cause a temporary black and blue spot; rarely the vein may clot. The risk of infection is slight. Some people faint when they blood drawn.

A total of about19 tablespoons (292 milliliters) of blood will be drawn over the entire course of the study. The total amount of blood taken for this study will be a little more than half of the amount taken for a routine Red Cross blood donation.

Risks of Genvoya:

Information from previous studies showed that Genvoya can be associated with nausea, headaches, diarrhea and fatigue. Most of these side effects were considered mild in nature.

Laboratory abnormalities that have been described with Genvoya include: elevations of blood levels of test used to measure kidney (creatinine) and liver function (ALT and AST). Some of these laboratory abnormalities were considered severe and occurred in more than 2% of studies participants enrolled in clinical trials with Genvoya.

Individuals taking Genvoya can experience an increase in a blood test that measures kidney function, known as creatinine. However, the increase in creatinine is not the result of kidney disease caused by Genvoya. Instead, Genvoya blocks the elimination of creatinine through the kidneys causing an increase in its blood levels. Most of the side effects associated with Genvoya occur when this medication is taken for a long time. It is unlikely you will experience toxicities with Genvoya since you will only take a total of two doses of this medication. You will also be monitored through the study to make sure that any side effect that you might experience is treated.

There may be side effects and discomforts that are not yet known.

5. Are there risks related to pregnancy?

Tenofovir alafenamide, one of the components of Genvoya, has not been evaluated during pregnancy. It is not known if some of the components of Genvoya are present in human breast milk. Therefore, pregnant women and women who are breast-feeding will not be allowed to participate in this study.

Because of the risks involved, you must use one of the birth control methods that you have discussed with the study staff. You must be using birth control when you start taking Genvoya. You must continue to use birth control until you stop taking Genvoya.

If you are not willing to prevent pregnancy, you will not be allowed to participate in the study.

This research may hurt an embryo or fetus in ways we do not currently know.

6. Are there benefits to being in the study?

There is no direct benefit to you from being in this study. If you take part in this study, you may help others in the future.

7. What are your options if you do not want to be in the study?

The alternative is not to take part of the study. You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

There are no costs for you if you decide to participate in this study.

9. Will you be paid if you join this study?

You will be paid a total of $900 for successful completion of the study - $80 of this payment is a bonus, which you will be eligible to receive if you complete all study visits as scheduled and have taken your medicines correctly.

If you leave the study earlier, you will be paid an amount proportional to the amount of the study you have completed.

All payments are made by check at the final study visit.

You will be provided with parking validation for the long Day 1 study visits, if applicable. You will need to bring your parking ticket with you to the study visit.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities**.**

If you decide to leave the study will be asked to complete a final safety monitoring visit that will include laboratory tests and clinical evaluation.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.

- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities**.**

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Hendrix at 410-955-9707. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?

If you think you are injured or ill because of this study, call the Principal Investigator Dr. Hendrix at 410-955-9707 during regular office hours. If you need to reach Dr. Hendrix after regular hours for emergencies you can page him at 410-283-1075.

If you have an urgent medical problem related to your taking part in this study, call Dr. Hendrix at 410-955-9707 during regular office hours and page him at 410-283-5898 after hours and on weekends. If you page Dr. Hendrix call 410-283-1075 and a**fter the tone, enter the phone number where you can be called, press the # key, and hang up.**

d. What happens to Data and Biospecimens that are collected in the study?

Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

16. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

_____

Signature of Physician/Mid-Level Provider (Print Name) Date/Time

_____

Signature of Participant (Print Name) Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

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