INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH

The Steady-State Pharmacokinetics of Dolutegravir/Rilpivirine Fixed Dose Combination (FDC) in Patients with End Stage Renal Disease (ESRD) Requiring Hemodialysis

Version 1.0

Supported by an unrestricted, investigator-initiated research grant
from ViiV Healthcare

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

TAKING PART IN THIS STUDY IS VOLUNTARY

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with your doctors or dialysis centers associated with IU Medical Center.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if severely low kidney function requiring dialysis affects the blood levels of the two component medicines in the HIV combination pill called JULUCA. This combination tablet is approved for use already by the FDA for treating HIV, but it is not approved for use in people with HIV needing dialysis. However, the FDA has approved the use of JULUCA in the patients in this study so we can determine how best to use it in patients needing dialysis, either for treating HIV or for preventing getting HIV if exposed to it from someone else.

You were selected as a possible participant because you are between 18-65 years old, do not have HIV infection, and either need to be on dialysis or have normal kidney function. Women who are pregnant or are breastfeeding are not allowed into this study. If you are needing dialysis, your dialysis doctor referred you to us or you responded to an advertisement. If you have normal kidney function, we expect you asked to be part of this study from hearing about the study from advertisements or from the patients on dialysis.

The study is being conducted by Dr. Samir Gupta, Dr. Zeruesenay Desta, and Dr. Allon Friedman, who are all members of the Department of Medicine at the Indiana University School of Medicine. The study is funded by the ViiV Healthcare, which is the company that makes JULUCA.

HOW MANY PEOPLE WILL TAKE PART?

If you agree to participate, you will be one of 20 people in Indianapolis, 10 who are on dialysis and 10 who do not have reduced kidney function.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to be in the study, you will do the following things at the following study visits:

Visit 1

At this visit, we will find out if you qualify for the study. You will be asked about your health and any illnesses you may have had in the past. You will be asked about medicines you are taking or have taken (including over-the-counter medicine, vitamins or herbal treatments). If you require certain medications, vitamins, or supplements, you may not be able to participate in this study or may need to space these apart from JULUCA. The study team will review how to take your medications with JULUCA to make sure you are comfortable with taking part in this study.

The study team will also collect information about you from your medical records and use it for this study. We will measure your height, weight, heart rate, blood pressure, and temperature and do a brief examination to make sure it is safe for you to participate. We will do a survey to assess your mood, as having depression prevents you from taking part in the study. We will then get blood specimens (about two tablespoons) from a vein in your arm (different from the one where your dialysis access is if you are on dialysis) to check to see if you are pregnant (if you are able to get pregnant), if you have HIV infection, if you have hepatitis B or C infections, if there are illegal drugs in your system, and to check your cell counts, kidney function, blood chemistries, and liver function. We will also do an electrocardiogram (ECG), which is to check your heart electrical rhythms, to make sure there is no contraindication to receiving JULUCA. Visit 1 will take one hour. This visit will take place at the Indiana Clinical Research Center at University Hospital.

It is possible that we will find that you are not suitable for this study based on the results of these screening tests. If this happens, your participation in this study will be complete.

Visit 2

Once we have all your test results from Visit 1 and determine you can safely continue in the study, we will ask you to return to review again your medication list and see how you are feeling. If you are capable of being pregnant, we will check for this once again.

If it still considered safe for you to participate, we will then provide you a supply of JULUCA and explain how to take these pills properly. You should take one pill per day, at about the same time each day, with a meal. JULUCA can be taken before or after a dialysis session, but JULUCA must NOT be taken during a dialysis session. We will also give you a diary to record when you take the JULUCA pills during the study. If you change your other prescribed medications, supplements, herbal remedies, vitamins or

any over-the-counter treatments during the course of the study, it is important that you notify the study team as soon as possible. It is important that no one else uses these JULUCA tablets.

Visit 2 should take 30 minutes. This visit will take place at the Indiana Clinical Research Center at University Hospital.

Phone Visits

Between Visit 2 and Visit 3, we will call you twice to check how you are feeling while taking JULUCA and to review the diary with you. We will also review your other medications again to make sure you are not receiving any new drugs that could interfere with the study. If there are any concerns about your safety or ability to properly take JULUCA during the study, we may stop your participation in this study. These phone visits will take no more than 15 minutes each time.

Visit 3

This is the main study visit where we will check the blood levels of the two medicines in JULUCA. You will come to the Indiana Clinical Research Center at University Hospital between 11 and 14 days since you started taking JULUCA. You must be fasting for 4 hours prior to arriving at the Research Center. Please bring your JULUCA bottle with you with all remaining tablets. We will once again review how you are feeling, any changes in your medicines, your JULUCA medication diary, and check your weight, heart rate, blood pressure, and temperature and repeat a brief examination. If all seems in order, then the study visit will continue. If there is any reason to believe that it is not safe for you to continue, or if we find you may not have taken the JULUCA pills properly, we may stop you from taking part in the study any longer or reschedule this study visit.

If it safe for you to continue, we will then place an IV (a small tube in an arm vein to draw blood). We will then take blood samples to check your blood counts, kidney function, blood chemistries, liver function, and the blood level of JULUCA. We will also obtain a DNA sample at this time if you permit us to do so. We will then give you a dose of JULUCA. We will then take blood samples 0.5, 1, 2, 3, 4, 6, 8, 12, 18, and 24 hours after this dose is given to check blood levels of JULUCA. The total amount of blood we will obtain at this visit will be about 6 tablespoons (8 tablespoons total for the entire study). After the 24 hour blood draw, you can leave the Research Center. You will no longer take JULUCA after Visit 3 is completed. Visit 3 will last as long as 26 hours.

Follow-up Visit

About 14 days after Visit 3, we will either call you or visit you during a dialysis session (if you are on dialysis) to see if you have developed any side effects since Visit 3 and to review your medication list one more time.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While participating in the study, the risks, side effects, and/or discomforts include:

Risks of taking JULUCA

The primary risks of JULUCA are listed below. There may also be side effects that we cannot predict. So it is important you tell us immediately if anything new feels wrong while on the study, especially if you feel tired/faint, feel pain in your stomach and don't want to eat, you bruise easily or develop itching, you develop yellow eyes/skin/urine, become confused, have trouble breathing or develop swelling. If these occur, we may have you return to the research clinic for evaluation and additional laboratory tests.

- Mental health disorders (worsening depression, insomnia, headache, thoughts of hurting yourself). Mental health disorders were the most common adverse events leading to discontinuation of JULUCA in clinical studies.
- Gastrointestinal disorders (nausea, vomiting, diarrhea, abdominal pain)
- Liver injury (including liver failure), jaundice
- Fever
- Skin reactions/rash and allergic reactions
    - Though very rare, a severe skin allergic reaction with fever, called a hypersensitivity reaction, can be life-threatening
- Harm to a fetus if pregnancy occurs
- Potential of laboratory abnormalities
    - Particular high blood sugar (hyperglycemia)
    - Pancreatic enzymes (lipase)

Other risks of being in this study include:

- Loss of privacy
- Risks of drawing blood (pain, bruising, infection, thickening of the vein)
- Unease when completing the mood questionnaire

To reduce the chances of these risks from happening:

- We will do everything we can to protect your privacy. All blood samples and study documents, except for this consent statement, will use a code number. All information will be stored in a password-protected computer file or secured in a locked cabinet in a keypad protected room.
- Blood will be drawn by experienced technicians.
- The mood questionnaire will be completed in a private setting; you can ask any question you like about the questionnaire.
- If you report having increased sadness during the trial or having thoughts of hurting yourself, we will make sure you get appropriate care.
- We cannot fully remove the risks or side effects of JULUCA, but we will:

- Only allow people who are considered at low risk of developing side effects into the study
- We will frequently be checking to see how you feel and make sure your other medicines will not interfere with JULUCA or increase the risks of its side effects. It is important that you do not take any other prescription drugs, over the counter medications or dietary or herbal supplements without first talking to your doctor(s) or study nurse. There is a risk of serious side-effects when certain non-study medications are taken with study drugs.
- We will ask you to use contraception or avoid sexual activity during the study to prevent any potential harms to an unborn child if pregnancy occurs

Are there risks if I get pregnant during the study?

Because the drugs in this study may affect an unborn baby, you should not take part in this study if you are pregnant or intend to become pregnant. There is a small risk that one of the components of JULUCA, the dolutegravir component, can cross from the mother's blood into the placenta and thus may cause brain or spine defects to a fetus early in pregnancy, even before you may know you are pregnant. So if you are a woman who can get pregnant, you must talk to your study doctor about birth control. You will need to use at least one of the following methods of birth control to prevent pregnancy to participate in this study. These include:

- Completely abstain from sexual intercourse with men throughout the study, OR
- Your partner is sterilized and is your only partner, OR
- Use one of the methods below in the correct way and in the same way every time, as instructed by your study doctor:

    - Any intrauterine device (IUD) approved by your study doctor because it has a low chance of failing to prevent pregnancy;
    - Hormonal methods to prevent pregnancy, like certain birth control pills, injections, patches or vaginal rings;
    - Any other method with a low enough chance of failing to prevent pregnancy approved by your doctor and the study.

Call the study doctor right away if you get pregnant during this study. You may be asked questions later about the pregnancy and the baby's health.

You should also note that if you become pregnant while receiving JULUCA, we will report this information to ViiV Healthcare and to the Antiretroviral Pregnancy Registry. We may need to follow-up with you throughout the pregnancy.

Mothers should not breastfeed a baby while on this study because the dolutegravir component of JULUCA can enter into breast milk.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?

We don't expect you to receive any benefit from taking part in this study, but we hope to learn things which will help scientists in the future help people on dialysis get treatment for HIV or protect them from being infected with HIV.

WILL I RECEIVE MY RESULTS?

We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, this information will be provided to you. We might learn about your HIV status or about problems with your blood counts, blood chemistries, kidney and liver function, or if you have depressed mood. We will provide you these results if they are abnormal or worrisome. If you wish to see these results even if normal, we will provide you a copy. You may need to meet with professionals with expertise to help you learn more about your results. However, the study team/study will not cover the costs of any follow-up consultations or actions. We will not provide you the results of the JULUCA blood levels.

HOW WILL MY INFORMATION BE PROTECTED?

Efforts will be made to keep your personal information confidential. All of your personal information will be recorded on paper records that will be kept secure in a room at our research clinic that can only be opened by our study team who have security badges. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the Indiana University Institutional Review Board or its designees, ViiV Healthcare, the Indiana Clinical Research Center (ICRC), and any state or federal agencies who may need to access your medical and/or research records (as allowed by law). State and federal agencies may include the Food and Drug Administration (FDA).

A description of this clinical trial is available on **ClinicalTrials.gov** (Record # NCT04431518) as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?

Information or specimens collected from you for this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

We may use your blood specimens to learn more about how the body uses JULUCA and how JULUCA is cleared by the body. We will store all blood specimens using only your study code and keep them in the research freezers of Dr. Zeruesenay Desta. The research freezer is kept in a locked room in the R2 Research Building at Indiana University School of Medicine. Only Dr. Zeruesenay and his study team have access to the research freezers in which your blood specimens will be stored. To protect you against the risks of loss of confidentiality, all samples including DNA samples will be marked with a unique code number. This information will be stored in an anonymous fashion in two different secured computer databases; one containing the sample codes and the other with your information (such as age, sex, ethnic group, health conditions, etc.) to maximize confidentiality. Samples from the freezers will be withdrawn by Dr. Desta's lab, which follows a logbook which include time and date of withdrawal and amount.

Making Your Choice

Blood and urine samples will be collected as part of your screening and/or during the study period. Please read each sentence below and think about your choice. After reading each sentence, circle or check "Yes" or "No" and add your initials next to the choice. No matter what you decide it will not affect your care. If you have any questions, please talk to your doctor or nurse or call our research review board.

Answering these questions will not in any way influence your eligibility to participate in the study. Eligibility criteria will only be evaluated on the exclusion and inclusion criteria outlined below. You retain (keep) the right to have any remaining sample material destroyed at any time by contacting the investigator. The investigator is responsible for the destruction of the sample at your request. However, any previously collected data from your sample cannot be destroyed.

1. My sample(s) may be kept for a period of up to 20 years or more for use in future research to learn more about how to treat health problems. This research may include testing how my DNA controls the way I respond to medicines like JULUCA.

   YES _____ NO _____

2. My sample(s) may be kept for a period of up to 20 years or more for use in research to learn more about the cause and prevention of health problems. This research may include testing how my DNA compares to other volunteers or to patients with a disease like HIV.

   YES _____ NO _____

3. Someone can contact me in the future to ask me to take part in more research.

YES _____ NO _____

WHAT WILL YOU DO WITH MY GENETIC INFORMATION?

The study data and results are for research purposes only. This research follows the Genetic Information Nondiscrimination Act (GINA), a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to request the genetic information we get from this research and to discriminate against you based on your genetic information.

We will not use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA. But we may use the DNA specimen to look at the genes responsible for how JULUCA is cleared by the body. We will not provide these results back to you.

WILL I BE PAID FOR PARTICIPATION?

You will be compensated for completion of two of the three in-person visits in this study. For Visit 1, you will be paid $50 upon completion of all study components for this visit. For Visit 3, you will be paid $250 after completion of all study components for this visit. You will not receive compensation for Visit 2. Payment will be in the form of a pre-paid gift card or by a refillable gift card.

WILL IT COST ME ANYTHING TO PARTICIPATE?

There is no cost to you for taking part in this study.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

WHAT FINANCIAL INTEREST DOES THE RESEARCHER HAVE?

The Principal Investigator, Dr. Samir Gupta, provides consulting services for the sponsor of this study. The Institutional Review Board (an ethics committee that helps protect people involved in research) has reviewed the possibility of financial benefit due to this relationship. The Board believes that the possible financial benefit to the study doctor is not likely to affect your safety and/or the scientific integrity of the study. If you would like more information, please ask the researchers or study staff.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher, Dr. Samir Gupta at 317-274-7926. After business hours, please call the on-call physician for University Hospital at 317-962-5000.

In the event of an emergency, you may contact Dr. Samir Gupta at 317-274-7926 or through the on-call physician for University Hospital at 317-962-5000.
If you are unable to reach the investigator at the above number(s) in an emergency, you may contact the University Hospital pharmacy at 317-944-0362 and ask them to page the IDS pharmacist on call.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

CAN I WITHDRAW FROM THE STUDY?

If you decide to participate in this study, you can change your mind and decide to leave the study at any time in the future. The study team will help you withdraw from the study safely. No risks are involved with stopping JULUCA. If you decide to withdraw, please contact the study coordinator or Dr. Samir Gupta. They will discuss returning JULUCA safely to the study team. Your future medical care will not be affected by your decision to leave the study.

Your participation may be terminated by the investigator without regard to your consent in the following circumstances: if the study team determines your safety is jeopardized by continuing to take JULUCA or undergoing the study procedures during Visit 1 or Visit 3; and if the study team determines you are not taking JULUCA as directed by the study team's instructions.

PARTICIPANT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____ **Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____ **Date**:_____