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INFORMED CONSENT TO BE ENROLLED IN 'ESTUDIO OPORTUNIDAD'

Study Title for Study Participants: Estudio Oportunidad

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Estudio Oportunidad: Optimizing Screening for Cervical Cancer Among Women Living with HIV in the Dominican Republic

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Key Information about 'Estudio Oportunidad'

You are invited to participate in a research study. It will evaluate new cervical cancer screening approaches compared with standard cervical cytology (Pap smear) among women living with HIV in Santo Domingo, Dominican Republic.

Women who join the study will be asked to attend three study visits over 2 years. Each annual visit includes two screening tests: 1) human papillomavirus (HPV) testing and 2) a standard Pap smear. Women with positive screening test results will be asked to come back for additional study visits if needed for further evaluations. Some of those women will need to receive treatment for precancer, which could cause side effects such as mild pain or discomfort.

You do not have to join this study. You could choose to receive standard cervical screening at other clinics. We will give you details about the purpose, procedures, risks and possible benefits related to this study. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We are inviting you to be in a research study

A research study is a way to learn new information. It is not the same as routine medical care. You are being asked to participate in this study because you are a woman living with HIV and are between 25 and 49 years old.

The purpose of this consent process is to give you the information you need to help you decide if you want to participate in the study. Please review this information carefully. You can ask questions at any time. When we have answered all your questions you can decide if you want to participate. You will be given a signed copy of this form to keep.

Why is the study being done?

The purpose of the Estudio Oportunidad is to compare different approaches to cervical cancer screening. In this study we will collect detailed information on human papillomavirus (HPV) infection and associated lesions on the cervix that could be an early sign of cervical cancer. HPV infection is very common, and for many women HPV infections and lesions can resolve without treatment. This study will help us identify which tests are most useful for screening.

HPV is more common among women living with HIV, and HPV lesions can be harder to treat for them. For this reason, cancer of the cervix or neck of the womb is more common among women living with HIV. With screening tests, it is possible to identify HPV infection and observe cervical changes early, before lesions get big and difficult to treat. This study will enroll women living with HIV to compare different approaches to cervical screening among women who may benefit most from receiving the highest quality screening test. The standard or usual approach for cervical cancer screening in the Dominican Republic is to detect changes in the cervix through a Pap smear.

In this study we will conduct a Pap smear (the usual approach) as well as newer screening approaches, such as detection of several types of HPV. Some HPV types are associated with early detection of precancerous lesions. The HPV test will be conducted on two different samples, one cervical sample collected by the study doctors, and one vaginal sample collected by the participants.

Women with a positive Pap or HPV test, will be asked to attend additional clinic visits. In addition to the usual examination after a positive screening test, which includes using magnification to inspect the cervix (called colposcopy), the study doctors will conduct two other new tests. First, we will conduct a laboratory test similar to a Pap test called “dual-stain cytology.” Dual-stain cytology helps to identify cells that are not normal and can be early markers of precancer. Second, the study doctors will take digital images of the cervix. These images can assist in detecting relevant changes associated with cervical precancerous lesions or cancer.

We will let you know if the Pap or HPV test was positive. The results from the additional study tests (specific HPV types, dual-stain cytology, and images of the cervix) will not be reported back to you as they are research results. They are being evaluated in this study to see if they can be used routinely in the clinic to manage patient care. Women with a positive Pap smear or HPV test will also be asked to contribute a small piece of tissue from the cervix (called a biopsy) to confirm the accuracy of the tests. We plan to include 600 women living with HIV in the study and will follow study participants for 2 years.

Who is organizing this study?

Estudio Oportunidad is being implemented by the Instituto Dermatologico Dominicano y Cirugía de Piel (IDCP) and Instituto Nacional del Cáncer Rosa Emilia Sánchez Pérez de Tavares (INCART) in the Dominican Republic. The study has public funding from the National Cancer Institute (NCI), part of the

National Institutes of Health (NIH) in in the United States Department of Health and Human Services, Bethesda, Maryland, USA. The scientific sponsor is the Fred Hutchinson Cancer Center in Seattle, Washington, USA.

Taking part in the study is your choice

- Your participation in this study is voluntary. You do not need to be in the study if you do not want to.
- If you choose not to be in this study, it will not affect your option to receive free HIV care at SAI (Servicios de Atencion Integral a Pacientes con Virus de Inmunodeficiencia Humana (VIH)).
- Even if you say yes and agree to participate now you can stop participating at any time.

This informed consent document has information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the pros and cons of taking part in the study. It's important that you have as much information as you need and that all of your questions are answered.

How long would I be in the study?

All study visits will take place at IDCP over 2 years. The number of study visits depends on your screening test results during the study. Participants will have at least three visits during the study.

What will happen if I decide to take part in the study?

<u>At your first visit at IDCP (about 2 hours)</u>

1. An interviewer asks you questions about your age, race, ethnicity, marital status, education, and history of cervical cancer screening and HIV, and recent sexual behavior.
2. You will be asked to provide your phone number and address so we can stay in contact with you during the study. We also ask for contact information for two trusted individuals (friends or family members) who we can contact if we are unable to reach you directly during the two years of the study.
3. A nurse collects 10mL of blood. We may use this to test your current HIV viral load and CD4 count if we cannot get this information from your HIV clinic.
4. You are given instructions and a private space for "self-sampling." This involves inserting a small soft brush, similar to a mascara wand, into your vagina to collect a small number of cells.
5. A doctor performs an exam of your pelvic area and cervix in a private room. The doctor will use a special tool called a vaginal speculum to better see your cervix.
6. During the exam the doctor uses a small brush to collect a very small number of cells from your cervix and also collect a small sample from your anal area. This is called "provider-sampling."
7. The samples of cells collected will be examined at a study laboratory using several tests including a Pap smear and HPV testing.

8. The study team will call you within 20 working days to share the results of the Pap smear and HPV tests. If your test results are not available within 20 working days, the study team will call you to let you know when they will become available.

Subsequent study visits for women with negative screening test results (about 1 hour)

1. After the first study visit, we ask that you return to IDCP two more times over 2 years. These study visits take place at approximately 12 and 24 months after your first visit.
2. We will repeat the interview, vaginal self-sampling, pelvic exam, and cervical provider-sampling at each visit. If the results of your study visits are negative, there will be a total of three study visits. If one of the screening tests is positive at any of the three visits, you will need to schedule a follow-up visit, described below.
3. You will be asked to provide a urine sample for use in future studies.
4. Between the study visits, IDCP study staff will contact you by phone call or WhatsApp, as you prefer, to follow-up with you and confirm your contact information.

Follow-up visits for women with a positive screening test results (about 1 hour)

If any of your screening tests are positive, we ask that you return to IDCP in about 2 weeks for a follow-up visit. Here is what will happen at that visit:

1. A doctor will conduct a more detailed physical examination of your cervix using a special light and lens to help make your cervix look bigger and easier to examine. This is called a colposcopy.
2. During the exam the doctor takes digital images (pictures) of your cervix using a medical camera. These images will be used in two ways. The first is to document any changes to your cervix during the study. Second, these images will be used in future research to help build a special computer program that can detect important cervical changes accurately. All of the digital images will be identified by a unique code number and not by your name.
3. The doctor will collect cells from your cervix for a special type of Pap smear called dual-stain cytology. This test helps to identify cells that are not normal.
4. The doctor will collect a biopsy from your cervix. This involves removing a small amount of tissue. It will feel like a pinch. This tissue will be examined under a microscope by a specialist. Depending on the results of this biopsy you may need treatment for cervical pre-cancer. The study team will call you in 20 working days to tell you the results of biopsies and plan next steps if treatment is needed. If your test results are not available within 20 working days, the study team will call you to let you know when they will become available.

If you have a negative biopsy indicating that you do not need treatment, we ask that you return to IDCP once per year for 2 years to repeat the interview, vaginal self-sampling, pelvic exam, and cervical provider-sampling. The next visits are approximately 12 and 24 months after the first visit.

Treatment visit for women with positive biopsy (about 1 hour)

1. The size and types of cervical lesions inform the doctor's selection of the treatment options that are best for you, which she will discuss with you.

2. One treatment, called thermal ablation, is the standard of care treatment for early lesions. During thermal ablation a doctor uses a portable device to apply heat to abnormal cells or lesions on the cervix. Most women experience little to no pain with thermal ablation.
3. The study team will call you 1 day and 1 week after your treatment visit to make sure you are okay.
4. If the doctor recommends more extensive treatment, she will discuss next steps and may refer you to another center for treatment.

We ask that you to return to IDCP once per year for 2 years to repeat the interview, vaginal self-sampling, pelvic exam, and cervical provider-sampling.

Treatment for women with advanced lesions at INCART (time and visits may vary)

If the pelvic exam by the doctor or biopsies show that you need more advanced treatment, we will make a referral to Instituto Nacional de Cáncer Rosa Emilia Sánchez Pérez de Tavares (INCART) in Santo Domingo. At INCART you will receive the care you need according to national guidelines for treatment. You would sign a separate consent form to receive treatment at INCART. The costs of this treatment will be covered by your insurance or a social assistance program.

A member of the Estudio Oportunidad team will be available to help you navigate care at INCART. Depending on the diagnosis and treatment you receive at INCART, you may be invited to complete additional study visits at IDCP for Estudio Oportunidad.

What are possible risks and discomforts I may experience as part of this study?

Feeling nervous or worried

You may feel nervous about answering questions, having a pelvic exam, getting your screening results, biopsy test results, or getting treatment for cervical lesions. Many women feel some anxiety about getting tests done and the possible results. You can discuss your fears and questions with a study staff person at any time.

Risks of having a blood draw

Blood tests can cause mild discomfort, bruising and/or bleeding at the blood draw site. Less likely is the possibility of feeling faint, or having significant bleeding, or infection.

Risks of having a biopsy

If you have a biopsy or biopsies of your cervix, you may feel brief pain like a pinch. Afterwards you may have some cramping and some spotting or bleeding for a day or two.

Risks of treatment for early cervical lesions

Significant safety concerns or adverse events in response to thermal ablation are not expected as these are reported to be infrequent and of low or moderate severity. However, you may feel mild pain or discomfort during the thermal ablation procedure. More serious, but rare, risks include heavy bleeding, infection, injury to the bladder or urethra, or accidental burns.

Privacy and confidentiality

Estudio Oportunidad will work hard to keep your identity and personal information confidential. Your answers to questions, lab test results, and all digital images will be identified by a unique code number and not by name. The link between your contact information and your unique code number will be kept in a locked file cabinet located at IDCP. Your contact information (phone number) will be used to keep in contact with you during the study and will only be used by study personnel. We can send you SMS texts, call you on your phone or use WhatsApp, based on your preference. All paper records from this study will be destroyed after 3 years. However, there is always a small chance that someone who is not part of the study may see your personal information by mistake.

As part of this study, we may use WhatsApp to contact you, an application downloaded from the Internet. The maker of the application may collect and store personal information, such as health information, location data, and internet usage. A complete description of what data will be collected and what the company will do with it can be found in the Terms of Service. You will need to agree to the Terms of Service to participate in this study if you are using WhatsApp for study communication, which is your decision. The researchers in this study may not have any control over what the company does with your information. The application and/or device may collect and transmit more information to the company than is needed for this study. If you do not want to be contacted through WhatsApp, we will contact you by phone or email if you prefer.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your results of study tests, will be kept in a central research database. However, your name and contact information will not be put in the database. If information from Estudio Oportunidad is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group. When data are shared your name or identity will be not be included.

Some of these organizations are:

- Every health care provider who provides services to you in connection with this study.
- Any laboratories or other individuals/organizations that analyze your health information in connection with this study as defined by the protocol.
- Study staff at Fred Hutchinson Cancer Center.
- Office for Human Research Protections (or OHRP). The OHRP provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research.
- U.S. Food and Drug Administration.
- Institutional Review Boards (or IRBs). IRBs are groups of people who review the research with the goal of protecting the participants who take part in the study. IRBs for this study include Fred Hutchinson Cancer Center, Instituto Dermatologico Dominicano y Cirugía de Piel (IDCP), and Consejo Nacional de Bioetica en Salud (CONABIOS).
- The study financial sponsor, the US National Cancer Institute (NCI) and NCI agents and partners.
- The National Cancer Institute will obtain information for this clinical trial under data collection authority Title 42 U.S.C. 285.
- A summary of the study results will be shared on www.ClinicalTrials.gov as required by United States law.

What are my other choices for cervical cancer screening if I choose not to participate in the study?

If you do not want to be in this study, you have the option to access a Pap smear for screening of cervical cancer through the Servicio Nacional de Salud (SNS) or with a provider of your choice.

What possible benefits can I expect from taking part in the study?

By participating in Estudio Oportunidad, you would receive three free comprehensive screening exams for cervical cancer over a two-year period. If you need treatment for early lesions we will assist you in receiving it at IDCP or in our collaborating centers as soon as possible. The results of this study may help improve cervical cancer screening approaches for women living with HIV in the Dominican Republic and in other countries.

What are the costs to participate in the study?

There are no direct costs to participating in the study. Medical costs for care you receive outside the study must be covered by you, your health insurance, or a social assistance program.

Compensation for your participation

You will receive a total of 600 DP (Dominican Pesos) as a transportation stipend for each scheduled study visit at IDCP.

Who do I contact if I have questions?

If you have any questions or need to report a study-related injury you can contact the Principal Investigator at IDCP, Dr. Yeycy Donastorg at 809-684-3257 ext 346 or 809-430-8925. You can also contact the Study Coordinator, Dr. Flavia Lantigua at 809-684-3257 ext 342 or 809-269-1351.

If you have any problems or questions about your rights as research participant you can contact Dr. Juan Periche, Coordinator of the IDCP Ethics Committee at 809-684-3257 ext 235.

Can I stop participating?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study team know as soon as possible so you can stop safely and get any treatment you may need. Any study data collected before you stop the study may be used by the study team. If you choose to stop study participation, it will not affect your option to receive free HIV care at SAI (Servicios de Atencion Integral a Pacientes con virus de inmunodeficiencia humana (VIH)).

Can I be removed from the study?

Yes. The study team may ask you to exit the study if:

- Your health changes.
- You do not follow the study rules.
- Participating in the study is no longer in your best interest.
- The study is stopped early by the study sponsor or IRB.

If you become pregnant after the study begins you can remain in the study. Treatment of cervical lesions in any woman who is pregnant may be delayed until the pregnancy has ended.

Access to medical records

As part of your participation in this study we would also access select information from your medical records at the SAI clinic, such as information on use of antiretroviral medication (ART) and results from recent blood tests like HIV viral load and CD4 count. If you receive care and treatment at INCART, we will access selected information from your medical records collected by INCART.

Storage for Possible Future studies

This section is about your choice to allow your stored samples and images from this study to be used in future studiesthough we do not currently have specific future study plans. If you agree, the following may be stored for possible use in future HPV-related research:

- Digital cervical images
- Remaining blood and urine samples
- Remaining cervical, vaginal, and anal specimens

- Questionnaire data
- Health-related information such as study test results or medications

You may decide that you do not want your samples to be stored for future research. If you decide that you do not want the remaining samples to be stored for future use, you can still participate in the current study and all remaining samples after completion of the study-specific tests will be destroyed. The analyses that would be carried out with the samples will be for research purposes only. The benefit of using stored sampled and data to conduct research includes moving the science forward to improve cervical cancer screening.

Storing samples for future studies is called "biobanking." Samples from biobanks may be shared with other researchers to make it possible to do more research that may improve people's health. Researchers who want to get samples and data from the biobank must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting approval to conduct future studies on the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you. The Principal Investigators on this protocol will review all future research requests, including their funding, scientific sponsors, and the Institutional Review Boards.

When the study team shares stored samples or images, they will be marked with a unique code number. None of the stored samples or images will contain any information that could identify you. For example, your name and identifying information will be removed from the information that is shared for any future studies. All future studies using stored samples will be conducted in a way that protects the rights and privacy of study participants.

If you decide to authorize the storage of samples for future research, you can change your mind at any time. If you change your mind, you should contact the study team and inform them that you no longer want your samples to be stored for future research.

If you decide to revoke your consent in the future, stored samples that were not used will be destroyed. However, information obtained from samples before you withdrew your consent will not be deleted. If you revoke your consent to store the samples for future use, you will be able to continue to participate in the current study and will not lose any benefit, medical treatment, or legal rights to which you are entitled.

What if you get sick or hurt after you join this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can. For all other medical problems or illness related to this research, immediately contact Dr. Yeycy Donastorg or Dr. Flavia Lantigua. They will treat you or refer you for treatment.

Study participants will not be charged for any expenses for treatment of an injury received due to their study participation. Medical costs for treatment will be covered by either the national health insurance (Servicio Nacional de Salud (SNS)) or internal social assistance programs specific to the hospital.

You will not lose any legal right to seek payment for treatment if you sign this form.

STATEMENT OF CONSENT AND SIGNATURES

I have read this form or had it read to me. I have discussed the information with study staff. My questions today have been answered. I know who to contact if I have questions or concerns in the future. I understand that my decision whether or not to enroll in Estudio Oportunidad is voluntary. I understand that if I decide to enroll I may withdraw at any time. By signing this form I do not give up any rights that I have as a research participant.

Name of participant: _____

Signature of the participant: _____ Date: _____

ACCESS TO HIV RECORDS

Please initial and date one option:

_____ I DO agree that my HIV data from SAI (Servicios de Atencion Integral a Pacientes con VIH) may be accessed and included in the study database.

_____ I DO NOT agree that my HIV data from SAI (Servicios de Atencion Integral a Pacientes con VIH) may be accessed and included in the study database.

ACCESS TO CERVICAL DIAGNOSIS AND TREATMENT RECORDS

Please initial and date one option:

_____ If I receive care at INCART, I DO agree that my diagnosis and treatment data from INCART may be accessed and included in the study database.

_____ If I receive care at INCART, I DO NOT agree that my diagnosis and treatment data from INCART may be accessed and included in the study database.

DIGITAL IMAGES OF THE CERVIX

Please initial and date one option:

_____ I DO agree that digital images of my cervix may be taken as part of the current study.

_____ I DO NOT agree that digital images of my cervix may be taken as part of the current study.

STORAGE FOR POSSIBLE FUTURE STUDIES

Please initial and date one option:

_____ I DO agree to the storage of my data and the biobanking of my samples for future research on HIV, HPV, and HPV-related diseases.

_____ I DO NOT agree to the storage of my data and the biobanking of my samples for future research on HIV, HPV, and HPV-related diseases.

RECRUITMENT TO ENROLL IN FUTURE STUDIES

Please initial and date one option:

_____ I DO agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

_____ I DO NOT agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

SIGNATURE OF WITNESS *(if needed for participants unable to read or write)*

By ticking the boxes and signing below I am serving as a witness on behalf of the participant. I confirm I have a trusted relationship with the participant. I am not associated with the research team.

The participant's questions have been answered.	Yes ☐	No ☐
The participant understands her rights and has provided informed consent.	Yes ☐	No ☐
The participant has been given a signed copy of this informed consent form	Yes ☐	No ☐

Signature of the witness: _____ **Date:** _____

CONFIRMATION OF ELIGIBILITY (*to be completed by the study site team member).*

Have you discussed the research study, procedures, and risks with the participant?	Yes ☐	No ☐
Do you believe the participant has provided voluntary and informed consent?	Yes ☐	No ☐
Have you confirmed the participant meets all the eligibility criteria?	Yes ☐	No ☐
Have you given the participant a signed copy of this informed consent form?	Yes ☐	No ☐

Name of study site team member: _____

Signature of study site team member: _____
Date:_____