**SUMMARY OF CHANGES**

**A Randomized, Phase III Study of Intra-anal Imiquimod 2.5% vs. Topical 5-fluorouracil 5% vs. Observation for the Treatment of High-grade Anal Squamous Intraepithelial Lesions in HIV-positive Men and Women**

**Version 8.0**

NCI Protocol #: AMC-088
Local Protocol #: AMC-088

NCI Version Date: 02AUG2023
Protocol Date: 02AUG2023

## I. Scientific and Substantive Changes:

| # | Section | Comments |
|---|---|---|
| 1. | Why is this study being done? | Accrual target was updated from 118 participants to 88 participants because of the slow accrual rate. |

## II. Administrative and Editorial Changes:

| # | Section | Comments |
|---|---|---|
| 2. | Global | The ICF was updated from version 7.0 to version 8.0 and the date was updated from 28JAN2022 to 02AUG2023. |

# MODEL INFORMED CONSENT

**Study Title for Study Participants:** Self-applied 5-fluorouracil Cream compared to Observation alone for the Treatment of Anal pre-cancers in HIV-positive Men and Women

**Official Study Title for Internet Search on http://www.ClinicalTrials.gov:** A Randomized, Phase III Study of Intra-anal Imiquimod 2.5% % vs. Topical 5-fluorouracil 5% vs. Observation for the Treatment of High-grade Anal Squamous Intraepithelial Lesions in HIV-positive Men and Women

**A Clinical Trial of the AIDS Malignancy Consortium (AMC)**

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## WHAT IS THE USUAL APPROACH TO MY ANAL PRE-CANCER, OR HSIL (HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESIONS)?

You are being asked to take part in the study because you are an adult with HIV and you may have, or have anal high grade squamous intraepithelial lesions (anal HSIL). Anal HSIL is tissue in the anal canal that has been damaged by infection with human papillomavirus (HPV) and is at risk for turning into cancer of the anus. Treating anal HSIL has been shown to lower the risk of developing anal cancer.

The standard of care (the accepted standard of treatment) for anal HSIL varies among treatment centers. Some of the ways doctors may care for people with anal HSIL include:

- Remove the anal HSIL lesions with a surgical procedure or other methods.

## WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach described above.
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for anal pre-cancer.
- Or you may choose to receive 5-fluorouracil outside of the trial.

## WHY IS THIS STUDY BEING DONE?

Anal HSIL is more common in men who have sex with men (MSM) and people who are living with HIV. Some people with anal HSIL will develop cancer of the anus, and treating anal HSIL lowers the chance that anal HSIL will turn into cancer. If anal HSIL turns into cancer, the standard treatment is surgery or chemotherapy and radiation. Most treatment of anal HSIL uses destructive methods such as electrocautery or surgery.

This study will study a drug applied directly to the anal skin, also known as topical therapy. We want to know if this topical drug is effective at getting rid of anal HSIL. We also want to understand how well people are able to tolerate this treatment. The treatment is topical 5-fluorouracil (5FU), which is also known as EFUDEX. 5FU is approved for treating actinic keratosis (precancerous conditions of the skin not related to HPV), and for superficial basal cell carcinoma (a skin cancer not related to HPV). This drug is experimental when used to treat anal HSIL. A prior version of this study also included 2.5% imiquimod. This arm was stopped early because this drug was no longer available.

About 88 people will take part in this study.

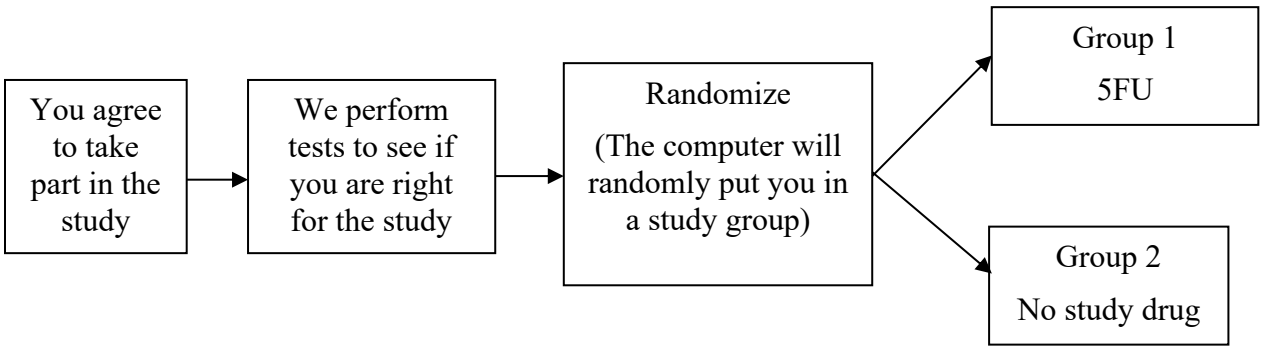
**WHAT ARE THE STUDY GROUPS?**

This study has two study group. If you are in the 5FU group, you will be asked to put on gloves and apply the cream to the inside of your anus using your finger or syringe.

- Group 1 will get 5FU.
- Group 2 will not get any study drug for the first 24 weeks.

A computer will assign you to one of the study groups by chance. This is called randomization. This is done by chance because no one knows if one treatment is better than the others. You have an equal chance of being in any group.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.




**HOW LONG WILL I BE IN THIS STUDY?**

If you are eligible and randomized, you will be in the study for up to 44 weeks.

**WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?**

Most of the exams, tests, and procedures you will have are part of the usual approach for anal HSIL. However, there are some extra evaluations that you will need to have if you take part in this study.

**Before you begin the study:**

We will ask you about your medical history and perform tests to confirm that you can take part. Your first visit will include the following unless done recently by a health care provider:

- Questions about your medical history, including:
  - Information about your HIV diagnosis and anal HSIL.
  - Whether you ever had an HPV vaccine (like Gardasil® or Cervarix®).
  - Your current medications, any history of allergies to medications.
- Extra tests and procedures:
  - A physical exam.

- A pregnancy test, if you are a woman who could become pregnant. Women also need to have a routine gynecologic exam within the last year.
- An anal cytology (Pap test) to test for abnormal cells in the anus. The researcher will insert a swab (similar to a Q-tip™) into your anus. The end of the swab will be rubbed against the skin inside the anus.
- A rectal exam with a finger to feel for any abnormalities.
- An anal exam called high resolution anoscopy (HRA) that uses a special microscope and dyes to find abnormal areas of the anus. A lubricated plastic anoscope will be inserted into your anus. Then, a swab moistened with acetic acid (i.e. vinegar) is placed in your anus so that abnormal areas will be visible. The researcher puts the anoscope back into your anus. A colposcope (a machine with a magnifying lens) is used to see the skin inside the anus. Iodine may be used to help make lesions show up.
- Biopsies to test anal HSIL. A biopsy cuts out a small piece of the abnormal skin (about the size of a sesame seed). Most often no medication to numb the skin is needed. If you feel pain, the researcher may inject a small amount of local anesthesia (Lidocaine or another anesthetic).
- Blood will be drawn (about 4 teaspoons) to check your blood cell counts. These tests will also measure your T-cells (part of your immune system that helps fight infections) and HIV viral load (how much HIV is in your blood).
- A blood test for HIV unless we have a copy of your HIV test results.
- We will ask you if you would like to donate blood to the AIDS and Cancer Specimen Resource. If you agree, you will sign another consent form. If you don't agree, you can still take part in this study.

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will be randomized to one of the arms described above.

- If you are in Group 1 (5FU). You will receive 16 weeks of treatment. Please bring back your containers of 5FU to every visit, even if they are empty.
- Four weeks after treatment stops, you will come to the provider's office for more tests.
- If you still have anal HSIL, your provider will discuss additional treatment options with you.
- About 11 months (44 weeks) after you started the study, you will be seen for final tests.

**If you are in Group 2 (no study drug):**

- You will be observed for 20 weeks (about 5 months).
- If you still have anal HSIL at week 24, you will have the option of receiving 5FU.
- You will receive 5FU from week 24 to week 40 (up to 16 weeks).
- About 11 months (44 weeks) after you started the study, you will be seen for final tests.

Study staff will follow you with HRA, anal biopsies, cytology and questions about how your are feeling. You will also undergo anal swabs for HPV testing. These tests are not part of the usual approach for anal HSIL. Neither you nor your health care plan/insurance carrier will be billed for

the collection of the anal HPV that will be used for this study. The anal HPV test results will not be given to you or your doctor.

*A study calendar that shows how often these tests will be done is attached.*

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information.

**WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?**

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- 5FU may not be better, and could possibly be worse, than doing nothing for your pre-cancer.
- **For all participants, there is a slight chance that HSIL can become cancer, requiring more involved treatments. The risk of progression to cancer is low in all arms. However, the risk is higher for those in the observation arm than in the 5FU group, since HSIL will be followed without treatment for up to 24 weeks.**
- **The risk of cancer during the time of no treatment is about 2 out of 1000 people. The risk of cancer with treatment is about 1 out of 1000 people.**

Anal Pap Smear and HPV Test: Insertion of anal swabs may cause some discomfort. Minor bleeding (less than a quarter of a teaspoon) occurs occasionally in men and women due to the insertion of the swabs. The bleeding stops almost right away.

HRA: Insertion of an anoscope will likely cause some discomfort. You may feel pressure and the urge to have a bowel movement. Putting acetic acid (vinegar) in the anal canal may cause some burning and irritation.

Anal Biopsies: You may have pain with the anal biopsies. You may have some bleeding for up to a week after biopsies, especially when you have a bowel movement. There is a rare chance of very heavy bleeding that may require extra treatment. There is a very slight risk of infection (<1%). Contact the study clinic if you have symptoms of heavy bleeding or infection (fever, redness, or swelling).

Injection of Local Anesthetic (numbing medicine): You may have a pinching or burning feeling from the shot of anesthetic. There is a very slight chance of reaction to the numbing medicine including rash, flushing, rapid heartbeat, and dizziness.

Blood Drawing (venipuncture) Risks: In many people, obtaining blood from a vein may cause some discomfort. This may include infection, bruising, and/or tenderness at the site where the blood is taken, and fainting or feeling faint.

Questionnaire: You will be asked questions about any sex you have had recently. Some people may find these questions embarrassing.

There is also a risk that you could have side effects from the study drug. Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The lists below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

**Study Group 1** - Table of Possible Side Effects of 5-FU for this type of cancer:

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving 5-FU, more than 20 and up to 100 may have: |
|---|
| • Pain, burning, irritation and itching<br>• Redness<br>• Swelling<br>• Ulcerations (i.e., sores on the skin) and bleeding<br>• Flaking and crusting of the skin<br>• Allergic reactions in the skin<br>• Pain, redness and sores on skin near the treatment area (for example on the scrotum in men) |

**Study Group 1** - In addition to side effects outlined above, people who are in Group 1 may also experience the possible side effects of 5FU listed in the Table below.

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving 5FU more than 20 and up to 100 may have: |
|---|
| • Scarring of the skin. |
| **OCCASIONAL, SOME MAY BE SERIOUS**<br>In 100 people receiving 5FU, from 4 to 20 may have:<br>• Emotional upset, insomnia, irritability<br>• Medicinal taste<br>• Low platelet counts, high white blood cells counts, and other blood count problems.<br>• Loss of hair, and other rashes.<br>• Red irritated eyes, and irritated nose.<br>• It may cause a herpes infection to return. |

| |
|---|
| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving 5FU more than 20 and up to 100 may have: |
| **RARE, AND SERIOUS**<br>In 100 people receiving 5FU, 3 or fewer may have:<br>• There have been miscarriages (loss of a pregnancies), and one birth defect (a serious heart condition) in women who have used 5FU during pregnancy. |

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The study drugs used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. If you are a woman and become pregnant or suspect you are pregnant while participating in this study, please inform your treating physician immediately. Women who could get pregnant and men who could father a child should use at least two forms of birth control for 3 months after stopping all study treatment.

**WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?**

This study has only a small chance of helping you because we do not know if the study drugs are effective. This study may help researchers learn things that may help other people in the future.

**CAN I STOP TAKING PART IN THIS STUDY?**

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest.
- If new information becomes available.
- If you do not follow the study rules.
- If the study is stopped by the sponsor, IRB or FDA.

**WHAT ARE MY RIGHTS IN THIS STUDY?**

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals*

*at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

**WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?**

The 5FU will be supplied at no charge while you take part in this study. It is possible that the 5FU may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

Your health plan/insurance company will need to pay for all of the other standard costs of treating your pre-cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for. If you do not have health insurance, arrangements may be made by the AMC to cover the cost of participation.

You will be reimbursed $100 per study visit for visits 1, 5 and 10 where anoscopies and biopsies are performed. You will receive $50 for all other visits while taking part in this study.

**WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?**

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

**WHO WILL SEE MY MEDICAL INFORMATION?**

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC)
- Any drug company supporting the study (Valeant Pharmaceuticals)
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S.

## WHERE CAN I GET MORE INFORMATION?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

## WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

## OPTIONAL SAMPLE COLLECTIONS FOR LABORATORY STUDIES AND DONATION OF LEFTOVER TISSUE SAMPLES TO THE AIDS AND CANCER SPECIMEN RESOURCE (ACSR)

### What is the usual approach to donate blood and/or tissue to the ACSR?

You are being asked to donate blood and/or tissue for future research. You are being asked to donate your blood and/or tissue samples to the ACSR because you have HIV infection and are being considered for participation in an AIDS Malignancy Consortium (AMC) clinical trial. The AMC works with the ACSR to collect donated samples from persons with HIV infection for research studies. People who do not take part in an AMC clinical trial can also donate samples to the ACSR.

### What are my other choices if I do not take part in this study?

It is your choice to donate or not donate your blood and/or tissue samples. You may still take part in the AMC clinical study if you choose not to donate blood or biopsy samples to the ACSR. You may also choose to donate:

- Blood but not tissue, or
- Tissue but not blood.

### What is the AIDS and Cancer Specimen Resource?

The ACSR is a biorepository (biobank) that collects human biological specimens (samples) from persons who have HIV or cancers related to HIV/AIDS. The ACSR stores the samples and some of the donor's medical information for use by researchers in future research studies. The National Cancer Institute (NCI) has set up the ACSR to assist researchers locate samples needed for their studies.

The ACSR has an independent research panel that approves researchers' requests to use the ACSR's stored samples for research studies. The ACSR only gives samples and medical information to researchers after their projects have been approved. Researchers may use the samples to study cancers and other diseases associated with HIV disease. This information may help us learn more about the causes of HIV-related diseases and cancers and to develop better ways to screen, diagnose, and treat them.

**Why is this study being done?**

The purpose of this study is to collect samples for the ACSR for future research studies. Researchers may study samples from the ACSR in combination with hundreds or thousands of other samples to explore how biologic or genetic factors may be related to HIV-related diseases and cancer. The information might help doctors in the future to identify who will or will not benefit from treatment. The samples may be used to learn more about how HIV-related diseases and cancers develop. The samples may also lead to new tests or discoveries. Finally, researchers may use the samples to study the genetic material from your cancer tissue and compare it to the material from your normal tissue (blood) to try to find the differences that exist. These studies could make it possible to identify many of the changes that are associated with diseases such as cancers. It may also help us tailor treatments to a patient's unique genetic make-up and/or to the genetic markers of the tumors.

**What extra tests and procedures will I have if I take part in this study?**

1. If you agree to donate blood, the medical team will draw about 2 tablespoons of blood to give to the ACSR. This takes about 10 minutes.
2. If you agree to donate tissue, your leftover tissue biopsy material will be donated to and stored by the ACSR.
3. Some of your clinical information will be released to the ACSR and entered into their database. The information given to the ACSR will not include your name or any information that could personally identify you.

**No extra biopsies will be collected for the ACSR.**

We will only give the ACSR tissue that is left over after making decisions about your treatment or diagnosis. The study doctor will not take any extra biopsies just for the ACSR.

We cannot tell you right now what future research these samples would be used for. Instead, we are asking that you give approval to give your samples for future testing without contacting you again. The results of whatever research is done on your samples will *not* be told to you or your doctor. The results of the tests will *not* be placed in your study records.

**How long will ACSR keep my samples?**

Your blood and/or tissue sample will be stored until it is used for research. The samples may be stored indefinitely.

**What possible risks can I expect from taking part in this study?**

- Blood Draw: The risks of drawing blood include temporary discomfort from the needle stick, bruising, and, rarely, infection.
- Biopsy: The risks of biopsy include possible need for stitches depending on the size of the biopsy. There may be swelling, slight pain and a small amount of blood loss. There is also a chance of infection at the site of the biopsy.
- Confidentiality: The ACSR will receive study samples with code numbers. There will be no personal identifiers on the samples. Then the samples will be re-labeled with a barcode and stored for future testing. While the ACSR and researchers who study ACSR samples will have no information that could identify you, there is a risk that someone could use information from

genetic studies to trace your samples back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

Let your study doctor know of any questions you have about these possible risks. You can ask the study doctor questions about side effects at any time.

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

This study is unlikely to help you. This study may help us learn things that may help people in the future.

The information may help to identify those who are at increased risk and those who may benefit from targeted treatment and screening. In turn, these studies could help find ways to prevent or improve treatments for HIV-related diseases and AIDS-related cancers.

**Can I stop taking part in this study?**

Yes, you may withdraw your samples from the ACSR at any time. You may contact your AMC study coordinator if you would like to withdraw your samples. The coordinator can ask in writing that your sample be removed from research use and that any identifiable sample and information still in their possession be destroyed. However, if any research has already been done using some of your samples, the data will be kept and analyzed as part of those studies.

**What are my rights in this study?**

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

**What are the costs of taking part in this study?**

There will be no cost to you for donating your samples to the ACSR. You will not be paid for taking part in this study.

**What happens if I am injured or hurt because I took part in this study?**

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The AMC will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to seek payment for injury even though you are in a study.

**Who will see my medical information?**

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC)
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Office for Human Research Protections and the National Cancer Institute in the U.S.

To protect your privacy, the AMC does not keep identifying information that links study participants to specific samples. As a result, the AMC and ACSR will not be able to link the results from studies that use your samples back to you. Thus, information, including genetic information, that researchers may obtain in studies that use your samples may not be directly linked to you and will not be placed in your medical record. However, some clinical and basic information obtained confidentially from the AMC will be attached with these data. It is possible that findings may one day help, for example, people of the same race or sex as you. It also is possible that genetic factors might come to be associated with people who have HIV and cancer through these kinds of studies.

**Where can I get more information?**

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at 1-800-4-CANCER (1-800-422-6237).

**Who can answer my questions about this study?**

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

Please circle your answer to show whether or not you would like to take part in each option:

1. **I agree to donate my blood to the ACSR for future research that may be used to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.**

   YES NO

2. **I agree to donate my blood to the ACSR for future research that may include genetic testing to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.**

   YES NO

3. **I agree to donate some of my tissue biopsy material that is not required for my treatment or diagnosis to the ACSR for future research that may be used to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.**

   YES NO

4. **I agree to donate some of my tissue biopsy material to the ACSR for future research that may include genetic testing to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.**

   YES NO

**MY SIGNATURE AGREEING TO TAKE PART IN THE MAIN STUDY**

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study *and any additional studies where I circled 'yes'.*

| | |
|---|---|
| _____ | _____ |
| Participant's Signature | Date of Signature |
| _____ | _____ |
| Signature of Person(s) conducting the Informed Consent Discussion | Date of Signature |

## AMC-088: STUDY CALENDAR FOR VOLUNTEERS

**5-fluorouracil cream to observation alone for the treatment of anal pre-cancers in HIV-positive Men and Women**

**Visit 1 (Baseline Visit, Enrollment, Randomization)**

At this visit, we will ask you about the following information and perform these exams:

- Any current anal problems and any symptoms you may have related to the anal HSIL
- Any changes to your medication
- Pregnancy test if you are female and able to become pregnant
- A physical exam
- A rectal exam with a finger to feel for any abnormalities
- High-resolution anoscopy (HRA) to document the size and location of your lesions. No biopsies are obtained
- It is important that you do not have anal sex or insert anything into the anus, including enemas, for 24 hours prior to each visit.
- A study nurse or doctor will ask you about smoking and recent sexual activity including how many sexual partners, use of condoms, and types of sexual activity.

We will take photographs of your lesions to document their appearance. A computer program will randomly assign you to 5FU, or observation group. If you are in the observation arm, your visit is complete. If you are in the 5FU arm, study staff will explain how to properly apply the treatment. You will be given a study diary to take home with you to help you remember any problems that you experience from the study treatment.

**Visits 2, 3, 4 (Week 2, 8, 16)**

At these visits, we will ask you about the following information and perform these exams:

- You will have a week 2 visit only if you are receiving 5FU.
- Your medical history will be updated for any changes since your last visit. This includes any side effects from the study exam, and any changes in your medication. A brief physical exam may be performed.
- Pregnancy test if you are female and able to become pregnant.
- A rectal exam with a finger to feel for any abnormalities.
- High-resolution anoscopy (HRA) at week 8. HRA may also be done at week 2 and 16 if your provider feels it is necessary to investigate symptoms you may be experiencing. Anal biopsies are only collected if it appears that the HSIL is getting worse.
- An anal swab for HPV testing will be done at weeks 8 and 16.
- Your treatment diary will be reviewed, and you should bring in any partially used containers of 5FU to be weighed. Empty bottles and tubes must also be returned for weighing.

**Visit 5 (Week 20)**

At this visit, we will ask you about the following information and perform these exams:

- Your medical history will be updated for any changes since your last visit. This includes any side effects from the study exam, and any changes in your medication. A brief physical exam may be performed.
- Pregnancy test if you are female and able to become pregnant.
- Anal swabs for cytology and HPV testing will be done.
- A rectal exam with a finger to feel for any abnormalities.
- A study nurse or doctor will ask you about smoking and recent sexual activity including how many sexual partners, use of condoms, and types of sexual activity.
- High-resolution anoscopy (HRA) to document the size and location of your lesions. At least 4 anal biopsies will be done to determine the extent of HSIL.

**Visits 6, 7, 8 and 9 (weeks 24, 26, 32 and 40)**

- For participants randomizedto 5FU, you will receive the results of the cytology and anal biopsies. If you still have HSIL, your study providers will discuss options to treat your HSIL other than study provided treatments. These treatments are not determined by the study. After you stop the study treatment, you will only need to return for Visit 10 at week 44 (not Visits 6, 7, 8 or 9).
- For participants randomized to observation, you will receive the results of the cytology and anal biopsies. If you still have HSIL, you have the option of being assigned to 5FU. This treatment would start at week 24. If you start 5FU at week 24, you will be asked to attend Visits 6, 7, 8 and 9. If you do not start 5FU, or if you do not have HSIL, you will only be asked to attend Visit 10 (week 44).
- Visit 6 (Week 24) has the same evaluations as Visit 1 (Baseline) except no HRA will be performed. If you agreed to donate blood to the AIDS and Cancer Specimen Resource, we will ask you to provide a blood sample again.
- Visits 7, 8 and 9 (weeks 26, 32 and 40) have the same evaluations as Visits 2, 3 and 4 (weeks 2, 8 and 16). Anal swabs for HPV testing will be obtained at Visit 8 (week 32) and Visit 9 (week 40).
- Your treatment diary will be reviewed, and you should bring in any partially used containers of 5FU to be weighed. Empty bottles and tubes must also be returned for weighing.

**Visit 10 (Week 44)**

This will be the final visit for this study. At this visit, we will ask you about the following information and perform these exams:

- Your medical history will be updated for any changes since your last visit. This includes any side effects from the study exam, and any changes in your medication. A brief physical exam may be performed.
- Pregnancy test if you are female and able to become pregnant.

- Anal swabs for cytology and HPV testing will be done.
- A rectal exam with a finger to feel for any abnormalities.
- A study nurse or doctor will ask you about smoking and recent sexual activity including how many sexual partners, use of condoms, and types of sexual activity.
- High-resolution anoscopy (HRA) to document the size and location of your lesions. At least 4 anal biopsies will be done to determine the extent of HSIL.
- If your biopsies show HSIL, your study providers will discuss treatment options available to you.

## AMC-088: AMC CERTIFICATE OF CONFIDENTIALITY

**Self-applied imiquimod gel or 5-fluorouracil cream to observation alone for the treatment of anal pre-cancers in HIV-infected Men and Women**

The NIH has given the AMC a Certificate of Confidentiality. The Certificate does not mean that the NIH or the U.S. Government recommend that you take part in this study. This Certificate helps us keep your health information private.

Your records for this study will have information that may identify you. This Certificate lets us turn down legal demands for your study records. We can use the Certificate to turn down demands for records from a U.S. court. The Certificate can be used in any federal, state, or local legal matters. We will use the Certificate to turn down any demands for your study records. The cases where we cannot use the Certificate are explained below.

We cannot use the Certificate to turn down a demand from the U.S. Government for study records. This applies to audits or reviews of the AMC. This also applies to study records that we have to report to the FDA.

The Certificate does not stop you or your family members from sharing your health information. It does not stop you from talking about taking part in this study. You may give written permission for an insurer, employer, or other person to get copies of your study records. If you give permission, we cannot use the Certificate to say no to a request for your study records.