



Clinical Investigation Consent Form The Rockefeller University Hospital

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The physicians at The Rockefeller University Hospital (RUH) and the Icahn School of Medicine at Mount Sinai (ISMMS) are engaged in research to examine the blood cells of the immune system (cells that are involved in fighting infection) in order to learn more about human immunodeficiency virus (HIV; the virus that causes Acquired Immunodeficiency Syndrome [AIDS]) and its effects on the immune system

You are being asked to join this research study, which will take place at RUH. This form tells about the research. You should ask questions of the person who is explaining this form to you. After you feel that you understand the research, if you want to be part of the study, you will be asked to sign the form. You can always ask more questions and can later change your mind about staying in the study.

If you join the research study, you will take part for about 48 weeks. The research study as a whole will last about 2 years.

About 20 people will take part in the research study.

Title of the research study: Simultaneous Disruption of Latency and Immune Enhancement by Poly ICLC during HIV-1 Infection

I. What this research study is about, and the reason for doing this research.

This study involves researching new approaches to treating HIV infection. Currently, HIV infection is treated with combinations of drugs called antiretrovirals. These drugs protect cells from infection by interfering with the viruses' ability to make copies of itself by infecting new target cells. Though these drugs are very effective, they cannot cure HIV infection and must be taken each and every day at prescribed doses to maintain their beneficial effect. In this research study we are investigating a new approach that involves an addition to existing medications.

We are investigating a medication called Poly-ICLC (Hiltonol®, Oncovir), which is an adjuvant. Adjuvants are medications that are designed to boost your body's immune responses resulting from a vaccine. We want to test whether Poly-ICLC is an adjuvant that



is safe and effective in HIV-infected patients. We are not giving a vaccine in this study, but just investigating the adjuvant, Poly-ICLC, to determine whether it is safe and may be useful in future vaccines that could be used to treat HIV, called therapeutic vaccines. One goal of future therapeutic vaccines is to reduce the virus that remains persistently inside of cells in a dormant or resting state despite treatment with HIV medications. This persistent pool is termed the “latent virus pool” or “viral reservoir”. One tactic to reduce this viral reservoir is to first stimulate HIV to start replicating in order to force it out of hiding. Once viral replication occurs, the infected cells may then be recognized and killed by cells of the immune system. Therefore, we also want to see what effect Poly-ICLC has on the virus that lives inside of cells. Specifically, we want to look at whether Poly-ICLC increases the level of virus inside your cells while also improving your immune system’s responses.

We are doing this research because we hope to find new ways to treat HIV infection that may reduce exposure to medications that are called antiretrovirals. Antiretrovirals are medications used to treat HIV infection. They are very effective but have side effects and have to be taken each and every day and cannot cure HIV.

We are asking you to take part in this research study because:

- You are between the ages of 18 and 55 and have been infected with HIV the virus that causes AIDS.
- You are currently taking medications to treat your HIV infection.
- Your level of virus in the blood has been below the level of detection (<50 copies/ml) for 6 months or longer.
- You are not pregnant, breast-feeding and do not plan on becoming pregnant for the duration of this study.
- You have never had a history of vascular disease including a heart attack, stroke, mini-stroke, or symptoms that could indicate you have these conditions.
- You have not smoked tobacco for more than 10-pack years.
- You do not have diabetes.
- You do not have elevated cholesterol that requires medication.
- You do not have a strong family history of heart disease.
- You have never taken immune based therapy for HIV and you are not currently taking medications that affect the immune system.
- You do not have drug-resistant HIV.
- You are not taking cancer chemotherapy.
- You do not have autoimmune disease such as lupus or rheumatoid arthritis.
- You do not have active co-infection with Hepatitis B or Hepatitis C.
- You have not participated in any other clinical trial within 30 days.
- You do not use drugs or drink alcohol excessively such that you would not be a reliable participant in the study.

Dr. Elizabeth Miller, Dr. Martin Markowitz and his associates at the Aaron Diamond AIDS Research Center (ADARC), an affiliate of the Rockefeller University (RU), will conduct this research. The clinical activities will be performed at the RUH. Laboratory studies will



be performed at ADARC and ISMMS as well as the Memorial Sloan Kettering Laboratories and QUEST Laboratories.

II. What is going to happen in this research study?

Consent Process: Informed consent is a process to help you understand the purpose of the research study, what will happen in the study, possible risks and benefits, and your right to withdraw from the study at any time. All of this information will be explained to you in detail. You should ask any questions you have until you feel that you understand what is asked of you to participate. You may then want to enroll, or you may decide not to join the study. The decision to participate is entirely up to you. Even after the study has started, you may at any time ask more questions, or decide to withdraw from the study.

In this part, we explain the meaning of words that we are going to use to describe this study:

“Substances drawn from your body” refer to **liquids** such as blood or urine.

Cells make up all parts of your body and are in your blood. The kinds of cells that are in your blood that we will be looking at are called white blood cells. DNA is inside all the cells of your body and carries your genetic or inherited information. When we draw blood or take other substances from your body, we are taking a **“sample.”**

“Cell line” means a group of cells that can live and grow outside of the body. They can also be frozen and can be used for future research.

This study has 2 phases.

They are:

1. Treatment Phase (2 days)
2. Observation Phase (48 weeks)

It is expected that you will participate in both phases of the study. However, you may withdraw at any time.

In order to participate in this study you must first have a screening evaluation. At the screening visit you will first sign this form indicating that you give consent to proceed with study procedures.

There are 2 screening visits. The first screening visit consists of a medical history and physical examination. You will be asked details about your medical history, current medications, allergies and your HIV infection. You may be asked to provide confirmation of the diagnosis of your HIV infection. If so, you will be provided with a separate form to obtain medical information from your primary care provider. You will have approximately 45 ml or 3 tablespoons of blood taken to check your blood counts, blood chemistries, liver



and kidney function, amount of virus in your blood and inside of your blood cells, and T cell count. You will also have a urinalysis and if you are a female of reproductive potential a urine pregnancy test. You will also have an EKG.

If the results indicate that you may be eligible for the study, you will be asked to return to the RUH for a second screening visit that will consist of a second blood test of about 30 ml or 2 tablespoons at least 5 days later to again test the amount of virus inside of your blood cells to determine your eligibility.

If you are found to be eligible for the study following the 2 screening visits and wish to participate you will be asked to return for the treatment phase.

Treatment Phase:

If you are eligible to enter the treatment phase you will be randomly assigned (i.e., by chance, using a computer program) to 1 of 2 groups, Arm A or Arm B. One group will get Poly-ICLC and one group will get placebo. You will have a seventy-five percent (75%) chance of being in the group that gets Poly-ICLC and a twenty-five percent (25%) chance of being in the group that gets placebo. Neither you nor your physician can choose the study group in which you will be assigned. Randomizations are done to avoid the chance that the results might be biased in some way. Neither you nor the study physician will know the group to which you are assigned until the completion of the study to avoid the chance that the results might be biased in some way. The group assignment will happen at the first visit of the treatment phase. One group, called Arm A will receive the Poly-ICLC. The second group is called Arm B and participants will receive an injection of placebo which is a salt or saline solution called normal saline.

The use of Poly-ICLC is experimental. Here, the word “experimental” means that the treatment is “not part of the usual routine care of patients”. In this study you may receive the experimental adjuvant called Poly-ICLC. The United States Food and Drug Administration (FDA) **has not approved Poly-ICLC for general use by the public.** However, we have told the FDA about this study, and it has allowed us to use Poly-ICLC in this study. A trained staff member will give the injection to you. The injection will be given under the skin (subcutaneously).

At the first study treatment visit, you will be asked how you are feeling, about specific health problems you may have had and any medications you are taking. You will have a limited physical examination. On the first visit, you will have approximately 5 and a half tablespoons or 80mL of blood drawn to measure blood counts, blood chemistries, kidney and liver function, amount of virus in your blood, measurements of immune responses, and measurements of the amount of virus in your blood cells. If you are female you will have a urine pregnancy test. After your blood and urine tests are performed, you will receive your first injection of either Poly ICLC (Arm A) or placebo (Arm B).



On the Day 2 study treatment visit you will be asked about specific health problems and or side effects you may have experienced from the first injection and any medications you have taken. You will have a physical examination. On the second visit, you will have approximately 5 and a half tablespoons or 80mL of blood drawn to measure blood counts, blood chemistries, kidney and liver function, amount of virus in your blood, measurements of immune responses, and measurements of the amount of virus in your blood cells. After your blood and urine tests are performed, you will receive your second injection of either Poly ICLC (Arm A) or placebo (Arm B).

Observation Phase:

You will have five visits following the treatment phase. At each of these visits you will be asked about specific health problems and or side effects you may have experienced from the previous injections and any medications you have taken. You will have a physical examination. At each of these visits you will have blood drawn. You will have tests to monitor your blood counts, blood chemistries, kidney and liver function, amount of virus in your blood, T cells, measurements of immune responses, and measurements of the amount of virus in your blood cells. You will have a total of 402 ml or approximately 2 cups of blood drawn during the observation phase over the five visits ranging between 73 and 83 ml (~ 5 to 6 tablespoons) per visit.

The following table summarizes all of the procedures that will occur during the course of the study:

Weeks	0		1-2				4	16	48
Days	Screen		1	2	4	8			
Complete history and physical	X								
Interval history and directed physical			X	X	X	X	X	X	X
Medication review	X		X	X	X	X	X	X	X
Chemistry and lipids	X		X	X	X	X	X	X	X
Blood Counts	X		X	X	X	X	X	X	X
Urinalysis	X								
Urine pregnancy	X		X						
HIV-1 RNA (Viral load)	X		X	X	X	X	X	X	X
T cells	X					X	X	X	X
Virus inside of cells	X	X	X	X	X	X	X	X	X
Blood for immune studies			X	X	X	X	X	X	X
Blood for immune cell gene expression			X	X	X	X			
Poly-ICLC or Placebo injection			X	X					
TOTAL BLOOD AMOUNT (ml)	43	30	80	80	80	83	73	73	73

YOU WILL CONTINUE YOUR ANTIVIRAL MEDICATIONS THROUGHOUT THIS STUDY. TAKING YOUR ANTIVIRAL MEDICATIONS 100% OF THE TIME IS VERY IMPORTANT TO DECREASE THE RISK OF DEVELOPING RESISTANCE TO YOUR ANTIVIRAL MEDICATIONS.



During the course of the study you will have blood drawn for many laboratory tests. Some of the tests you will have are considered routine and part of the care of people with HIV infection.

A New York State-approved laboratory will do these laboratory tests during the study. We will tell you about these test results that are performed and what they mean. These tests will be used to make clinical decisions about your treatment.

This is a research study and by law, we cannot tell you or your physician the results of any experimental tests. However, none of the experimental tests will be used to make clinical decisions about your medical condition or treatment.

In this study, you will receive routine care for any medical conditions related to your participation in this protocol unless these problems arise as a result of not following instructions on how to take medications and when to come to the clinic for appointments.

In this study, you will not receive routine care for any other medical conditions you may have.

Your medical information and some test results will be written in your Hospital chart. The researchers or the Sponsor of the study may also keep separate records with information about you and your study tests.

Sometimes we will need to look at your earlier medical records. We will ask you to sign a form that will let health care providers share your records with us. This could be your physician, a clinic or another hospital where you have been treated before.

III. What are the risks of taking part in this research study?

There may be some risks and discomforts in taking part in this study. We know that these risks and discomforts may happen during this study:

Blood draws: Blood will be taken by inserting a small needle in your vein by a trained staff member. You may feel discomfort, dizzy, or even faint when your blood is drawn. Redness, pain, swelling, bruising, or an infection may occur where the needle goes into your arm

Pregnancy and Contraception: **You are strongly discouraged from getting someone pregnant or becoming pregnant while participating in this study.** There may be risks to you or to your embryo or fetus if you become pregnant during the course of the study.

All sexually active study participants must use adequate and reliable forms of contraception.

You must either agree to abstain from intercourse or use one of the following double barrier methods of birth control:



- Male condom and spermicide
- Male condom and diaphragm
- Diaphragm and spermicide

OR

Any intrauterine device (IUD) or any other method with published data showing the lowest failure rate is less than 1% per year. If you are a female and are able to become pregnant, you must have a negative pregnancy test prior to receiving Poly ICLC injections.

All persons with HIV should use a double barrier method of birth control during sexual activity.

Hormonal birth control methods are not acceptable because their effectiveness is lowered by many of the antiretroviral drugs.

The effects of Poly ICLC on the reproductive system (sperm/egg development) and fetus are unknown.

If you become pregnant while on study following administration of Poly ICLC, we will continue to follow you for all follow up visits including a physical examination. We will also perform blood draws for follow up visits if you are not anemic and your blood pressure remains $\geq 100/60$. This will be performed in consultation with your primary care physician. If you do not have a primary care provider, Dr. Miller, Dr. Markowitz and associates will provide care until this is in place.

Treatment Phase

If you are randomized to Arm A, you will receive Poly ICLC (Hiltonol®, Oncovir) which can cause certain side effects. In the past, Poly ICLC has been administered by injection to more than 500 patients with cancer, either into the nose or by injection to more than 100 healthy volunteers, and by injection to more than 40 patients with HIV/AIDS who were not treated with antiretroviral medications or their virus was not suppressed by antiretroviral medications. The most frequently reported side effects associated with Poly-ICLC include: tiredness, fever, chills, redness and swelling at the injection site, infection at the injection site, increased overall inflammation in your body, pain in the muscles and joints, headache, elevations in liver function tests, and temporary lowering of the white blood cell count and the platelet count. White blood cells fight infection and platelets help your blood to clot. You will be closely monitored for these effects.

There may be an increase in production of your HIV inside of your cells and possibly increased virus levels in your blood. We cannot rule out that there could be unknown risks associated with increased virus production inside of your cells, including increased potential to transmit HIV to another person during this time and worsening of your HIV disease in the future. You will be closely monitored for increases in the level of virus in your blood. Should these levels rise at least 10-fold and remain elevated for at least 2



weeks or more, we will alter your antiretroviral medications in consultation with your primary care provider.

Observation Phase

There are no risks associated with this phase of the study other than those associated with blood drawing (as above).

Privacy Risks: There is the risk that there could be computer security breaches which could reveal your identity. There may be the risk that data about you may become public, and could be used by employers or law enforcement agencies. These privacy risks are described in greater detail below.

There may be other risks and discomforts that we do not know about now, but we will tell you any new information discovered which might affect your decision to participate or remain in the study.

IV. What are the alternatives to participating in this research study?

There are other procedures or treatments for your disease. If you join this study, you will not be able to get these procedures or treatments. If you want to receive these procedures or treatments, you should not join this study.

V. What are the benefits of taking part in this research study?

If you take part in this study, we do not expect there to be a benefit to you, but it is possible there will be a benefit to you. What we learn from this study may help others who have HIV in the future.

VI. Who will be able to see the information learned about you in this research study?

We will keep your personal information private, and will do our best to keep this information confidential. We will listen to what you say we may do with this information, and we will follow the law. For example, by New York State law, hospitals must inform the New York State Department of Health if we find that you have a reportable communicable disease, such as a sexually transmittable disease, like chlamydia, hepatitis, gonorrhea, syphilis and HIV-1. Also, the researchers must report to the authorities if they believe that child abuse or neglect has happened, or to prevent serious harm to you or others.

We will share information about you with our collaborators at ISMMS who are performing the immune response studies. We will also share information with the Sponsor, the Division of AIDS and other government agencies that oversee this research, and the people at the Hospital, ADARC and at The Rockefeller University in connection with their duties.



Whenever possible, data about you will be unlinked from your name and identified by a code. Sponsors receive your data linked only to a code. However, auditors and regulators from government agencies that oversee research, and people at the Rockefeller University Hospital and at Rockefeller University may see your information in the course of their duties.

During this study, only the researchers will know that your samples came from you, because your stored samples will be identified only by a special code instead of your name. As a result, others who study your samples will not know that they came from you and will not be able to figure out that they came from you.

If the researchers publish the results of this study, they will not mention your name or other information that could identify you.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, 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.

Genetic Information Nondiscrimination Act

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information is available in the outpatient or inpatient information handbook.

VII. What are the payment arrangements?

There is no cost to you for being in this research study.

You will receive free meals at study visits and metrocards for transportation upon request. At each of the last two study visits (weeks 16 and 48) you will be compensated \$50.00.

If research using your samples helps develop a drug or another product that is sold to the public, the drug company, the University and the researcher may share in some of the profits. For example, a cell line from your samples could be used to make a product for sale. There are no plans to pay you any money resulting from such discoveries. However, by signing this form, you do not give up any rights you may have.



VIII. What happens if you don't want to stay in this study or your participation is ended?

You can choose if you want or do not want to be part of this study. If you do not join, there is no penalty and no one will hold this against you. If you decide to join this study, you may change your mind and stop taking part in the study at any time, and this will not be held against you. Information about you up to that time may stay a part of the study.

During this study, the researchers may learn new information that might make you change your mind about whether you want to stay in the study. You will be given that information promptly.

If you decide to join the study now but later want to stop, you should let the researcher know.

The researchers also may stop you from taking part in this study, even if you do not choose to stop being in it. You may be asked to leave the study if you fail to follow instructions on how to take medications, if you do fail to keep your scheduled clinic appointments, if it is determined that your participation is dangerous to your health, if your health deteriorates during your participation, if the study is terminated by regulatory authorities or if you become pregnant.

IX. Consent to the use, storage and sharing of your samples or data for separate research studies

The scientific value of your samples and the information obtained from them is greatly increased if we can share them with other scientists at universities and pharmaceutical companies worldwide. May we store, use, and share your blood and/or tissue samples and data with other investigators at ISMMS, ADARC, Rockefeller and elsewhere for separate studies for many years? Your samples will either be stripped of information identifying them as yours or coded (we will hold the key to the code) so that they cannot be identified as having come from you. Other data related to your sample, but that does not identify you may accompany the samples.

Any time in the future, you may withdraw your consent to use any samples that have not already been used in research or shared. If you withdraw your consent, the remaining unused samples will be destroyed, unless the samples cannot be identified as having come from you.

Would you like us to store, use, and share your blood and/or tissue samples/associated data as described above?

Yes _____

No _____



If you say “no” to this question, this will not affect your participation in this study.

X. Who do you call if a medical problem results from this research study?

If you believe that this study has led to a medical problem, you should call the researcher listed below right away. The researcher will help you get appropriate, available medical care.

Name: Elizabeth Miller, MD
Phone No.: (212) 824-9246
Cell No.: 646-345-7774
Fax No.: (646) 537-9577

The Rockefeller University does not plan to pay for medical care that you may have as a result of taking part in this study at The Rockefeller University Hospital. However, you do not give up any rights you may have to seek compensation by signing this form.

XI. Who do you contact if you have questions about the research study?

Please ask as many questions as you want about this research study and this consent form. If you agree to take part in this study and have questions later on, contact the following researcher:

Name: Elizabeth Miller, MD
Phone No.: (212) 824-9246
Cell No.: 646-345-7774
Fax No.: (646) 537-9577

If you have any concerns about your experience while taking part in this research study, you may contact The Rockefeller University Institutional Review Board (IRB) Office at (212) 327-8410, or the Office of Clinical Research at (212) 327-8408.

XII. May we have permission to contact you about future studies?

May we contact you by phone to find out if you are interested in hearing about new research studies? Contact would be made by the Rockefeller staff of the Clinical Research Support Office for Recruitment. If you decide at any time that you no longer want to be contacted, please tell us, and we will stop calling you.

Would you like us to contact you about future research studies?

Yes _____ No _____

If you say “no” to this question, this will not affect your participation in this study.



AGREEMENT TO PARTICIPATE -- SIGNATURES REQUIRED

I have read this consent form, and my questions have been answered.

A copy of this consent form will be given to you. Please keep a copy of the form as it contains important information that you may wish to refer to during the research study and thereafter.

I hereby voluntarily consent to take part in this research study.

Name of the Study Participant (Print) _____

Signature of Study Participant

Date (To Be Filled in by Study Participant)

Signature of the Person Conducting the Informed Consent Discussion

I have explained the research protocol and this consent form to the participant and have answered the participant's questions about this research study and/or the consent process.

Name of Person (Print) _____

**Signature of Person Discussing
Consent**

**Date (To Be Filled in by Person Discussing
Consent)**