

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5258, Version 1.0, 12/17/08

Phase II, Double Blind, Randomized, Exploratory Study of Chloroquine for Reducing HIV-Associated Immune Activation

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

If you are seen at the Hospital of the University of Pennsylvania [HUP], your contacts are:

Principal Investigator:	Pablo Tebas, MD	(215) 349-8092
Coordinator:	Joseph Quinn, RN	(215) 349-8092
Study Nurse:	Wayne Wagner, RN	(215) 349-8092

24 Hour Emergency Number (215) 662-6059 Ask for the Immunodeficiency Program Doctor on call

Introduction:

You are being asked to take part in this research study because you are infected with human immunodeficiency virus (HIV), the virus that causes AIDS, and are not currently taking antiretroviral therapy (ART). This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is Pablo Tebas, MD. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Study Being Done?

The purpose of this study is to learn:

- How well chloroquine reduces the level of activity of your lymphocytes (cells that help fight against infection) and how this relates to progression of HIV disease.
- How well people infected with HIV tolerate chloroquine,
- How safe chloroquine is in people infected with HIV.

Chloroquine is approved by the Food and Drug Administration (FDA) for treating individuals infected with malaria (an infection spread by the bite of a mosquito). Chloroquine is not approved for the treatment of HIV infection. A placebo will be used to see how well the chloroquine works. A placebo is a "look-alike" inactive pill that does not contain drug.

What Do I Have To Do If I Am In This Study?

Screening

If you agree to join this study, you will be asked to sign this consent form. After you have signed the form, you will be asked some questions and will undergo some tests to see if it is safe for you to take part in the study. An HIV test may be required to document your HIV status. You may be asked to sign a separate consent form if you require an HIV test. The screening visit will last about 1-2 hours.

If you do not enroll into the study

If you decide not to take part in this study or if you do not meet the eligibility requirements, we will still use some of your information. As part of this screening visit, some demographic (e.g., age, gender, race), clinical (e.g., disease condition, diagnosis), and laboratory (e.g., CD4 cell count,

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

viral load) information is being collected from you so that ACTG researchers may help determine whether there are patterns or common reasons why people do not join a study.

Pre-Entry

Based on your screening evaluation, the study nurse will determine if you qualify for the study, and will ask you to come to the clinic for pre-entry evaluations. This visit must be separated from the screening visit by at least 24 hours and will last about 30-60 minutes.

Entry

You will also come to the clinic for entry evaluations. This visit must be separated from your previous visit to the clinic by at least 24 hours. This visit will last about one hour.

At this visit you will be randomized (by chance, like the flip of a coin) to one of the two groups listed below:

- Group A: 12 weeks of chloroquine followed by 12 weeks of placebo.

OR

- Group B: 12 weeks of placebo followed by 12 weeks of chloroquine.

You have an equal chance of being assigned to either group. Neither you nor the study staff will know whether you are in group A or group B. The study treatment chloroquine or placebo will be given to you at this visit. Chloroquine and placebo are provided by the study. You will take chloroquine (or placebo) once a day by mouth for a full 24 weeks. Once you have completed your assigned study treatment, you will come in for a follow up visit 4 weeks later.

Post Entry

After you start taking the study treatment, you will be asked to come to the clinic on weeks 4, 10, 12, 16, 22, and 24. At each visit you will receive enough study treatment to last until the next visit. It is very important to remember to return any unused medication at each visit, especially at week 12 when you will begin to take the next treatment for your assigned group. Each visit will last between 30 to 60 minutes.

Final Visit (Week 28)

Four weeks after you have completed taking the study treatment/placebo, you will be asked to return to the clinic for a final visit. This visit should last about 30-60 minutes.

Premature Discontinuation of Study Treatment

If you stop taking the study treatment before the end of the study, you will be asked to return to the clinic for additional tests. This visit will last about one hour. You will be asked to continue to be part of the study and attend study visits. If you do not agree to continue to come to the clinic for study visits, this will be your last visit. Coming off the study early will not affect the medical care you receive as part of your regular care.

If you are taken off study early or decide to leave the study early, you will be asked to return to the clinic for a final visit. This visit will last about 30-60 minutes.

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

The following table summarizes the study visits for the study and what tests will be done:

Evaluation	Screen	Pre-Entry	Entry	Wk 4	Wk 10	Wk 12	Wk 16	Wk 22	Wk 24	Wk 28
History and Background Tests	X		X							
Clinical Assessment	X	X	X	X	X	X	X	X	X	X
Physical Exam		X								X
Eye Exam	X					X			X	
Safety Labs	X	CBC ONLY	X	X	X	X	X	X	X	X
Pregnancy test	X		X	X	X		X			
CD4 and Viral Load	X	CD4 ONLY	X		X	X		X	X	
Special immunology test		X	X		X	X		X	X	X

Description of Evaluations

- History: At screening you will be asked about your medical and medication history; documentation of your HIV status will be obtained (or you will be tested today); CD4 nadir. In addition, you will have a 1 teaspoon of blood taken for G-6PD deficiency. This is a type of inherited anemia (low red blood count). A hearing test and an EKG will be performed. An EKG (electrocardiogram) is a test that measures your heart's activity. This is done by placing small stickers along your chest and arms.
- Clinical Assessment: The study staff will check your weight and vital signs such as temperature, blood pressure, and pulse. You will be asked about any medications you have taken since your last visit, if you have missed any doses of study treatment, and about how you are feeling.
- Physical Exam: You will have a complete exam by the study doctor.
- Routine Safety labs: About 1 tablespoon of blood will be drawn to monitor your CBC (complete blood count) and chemistries, including how your liver is working
- CD4 and Viral Load : About 1 tablespoon of blood taken from a vein in your arm for:
 - CD4+ and CD8+ cell count (number of white blood cells that fight infection)
 - HIV viral load test (a measure of how much HIV is in your blood)
- Special Immunology Tests: About 4-5 tablespoons taken and stored for immunology testing that is required for this study. These tests will look at your body's defense against illness and its reaction to the study treatment.
- Eye Exam: Have your pupils dilated (made larger) using eye drops and complete an eye exam with an ophthalmologist. (This test will be performed at screening, week 12 and week 24, but may be repeated at another visit if you or the study staff notice any change in your vision).

These evaluations which are done at screening may need to be repeated if changes are noted by you or the study staff during the study:

- Hearing test
- EKG (electrocardiogram).

It is important to remember that you should arrive fasting for the pre-entry, entry, and weeks 10, 12, 22, 24, and 28 visits. This means that you should not eat or drink anything for at least 8 hours before your visit. You may drink water and take your medications during this time. If you do not fast before these visits, you will be asked to come back fasting within 3 days to repeat some blood tests.

If you are a woman who is able to become pregnant, you will have a urine or blood (serum) pregnancy test at screening, entry, weeks 4, 10, 16 and whenever pregnancy may be suspected.

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

Pregnant women cannot enter the study. If a serum pregnancy test is completed an additional teaspoon of blood will be drawn.

You will be given the results of all pregnancy tests (if done), CD4+ and CD8+ cell counts, viral load, G-6PD deficiency, and routine blood tests as soon as they become available.

Other

All blood samples will be stored with the usual protectors of identity, such as assigning codes to the samples rather than names, storage in secure locations, and allowing only study staff to have access to your information.

Some of your blood (as noted above) will be stored and used for immunology testing that is required for this study. This blood will be stored for an indefinite length of time.

The total amount of blood you will have drawn for the entire study will be approximately 39 tablespoons.

Some of your blood that is leftover after all required study testing is done may be stored (with usual protectors of identity) and used for ACTG-approved HIV-related research. Storage of leftover blood is not a requirement to participate in the study, and you may withdraw your approval for the storage of your leftover blood at anytime. You may contact Joseph Quinn at 215 349-8092 if you wish to withdraw your approval. These samples may be held for an indefinite length of time. We cannot ensure that you will be told the results of the research done on these samples. Please indicate with your initials below whether you agree to have your leftover blood samples stored.

_____ YES

_____ NO

How Many People Will Take Part in This Study?

About 30 people will take part in this study nationwide. About 2-3 people are expected to participate at the University of Pennsylvania.

How Long Will I Be in This Study?

You will be in this study for about 28 weeks. (about 7 months)

Why Would The Doctor Take Me Off This Study Early?

The study doctor may need to take you off the study early without your permission if:

- the study is cancelled by the ACTG, the FDA, National Institutes of Health (NIH), the Office for Human Research Protections (OHRP), the drug company supporting this study, or the site's Institutional Review Board (IRB). (An IRB is a committee that watches over the safety and rights of research subjects.)
- the Safety Monitoring Committee (SMC) recommends that the study be stopped early (the SMC is a group of experts appointed by the ACTG Scientific Committee who monitor the study).
- you are not able to attend the study visits as required by the study.

The study doctor may also need to take you off the study drug without your permission if:

- continuing the study treatment may be harmful to you
- you need a treatment that you may not take while on the study

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

- you are not able to take the study treatment as required by the study
- you become pregnant or are breast feeding

If you must stop taking the study drug(s) before the study is over, the study doctor may ask you to continue to be part of the study and return for some study visits and procedures.

If I have to permanently stop taking study-provided chloroquine, or once I leave the study, how would chloroquine be provided?

If you must permanently stop taking study-provided chloroquine before your study participation is over, the study staff will discuss other options that may be of benefit to you.

After you have completed your study participation, the study will not be able to continue to provide you with chloroquine you received on the study. If continuing to take these or similar drugs would be of benefit to you, the study staff will discuss how you may be able to obtain them.

What Are The Risks Of The Study?

The treatment used in this study may have side effects, some of which are listed below. Please note that these lists do not include all the side effects seen with these drugs. These lists include the more serious or common side effects with a known or possible relationship. If you have questions concerning the additional study treatment side effects please ask the medical staff at your site.

There is a risk of serious and/or life-threatening side effects when non-study medications are taken with the study treatment. For your safety, you must tell the study doctor or nurse about all medications you are taking before you start the study and also before starting any new medications while on the study. Also, you must tell the study doctor or nurse before enrolling in any other clinical trials while on this study.

Risks With Use of Chloroquine

Some of the more common and severe risks of chloroquine are listed below:

The following serious side effects have been associated with use of chloroquine:

- Damage to the eye, which can lead to decreased vision and blindness and that can become permanent with long term or high dose chloroquine use
(The dose of chloroquine used in the study is not considered a high dose.)
- Deafness
- Muscle weakness
- Seizures
- Worsening of the medical condition psoriasis (a skin disease)
- Worsening of the medical condition porphyria (a rare blood disorder)
- Severe decreases in the number of cells in the blood including red blood cells, white blood cells, and platelets
- Abnormal heart rhythm (change in the way your heart beats)
- Decrease in heart function

In addition to the serious side effects listed above, additional side effects include:

- Blurred vision or trouble focusing
- Difficulty hearing or ringing in the ears

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

- Upset stomach, stomach cramping, or vomiting
- Diarrhea
- Loss of appetite
- Rash, which may include itching and swelling
- Increased skin sensitivity to sunlight (sunburning faster than normal)
- Change in skin color
- Tiredness
- Headache
- Loss or lightening of hair
- Mood changes such as depression
- Personality changes
- Confusion
- Decrease in blood pressure

NOTE: Children are very sensitive to chloroquine and even small doses can cause health problems including death. It is important to keep this medication out of reach of children.

Risks of Drawing Blood

Having blood drawn may cause discomfort, bleeding, and bruising where the blood is drawn. Occasionally, there is swelling in the area where the needle enters the body, and there is a small risk of infection. There is also a risk of lightheadedness, fainting, and blood clots.

Risks of Pupil Dilation

Dilation may cause you to experience sensitivity to light and blurring of your near vision. This may affect your ability to drive. Your eyes will remain dilated for 4 to 6 hours.

Are There Risks Related To Pregnancy?

The study treatment in this study may be unsafe for unborn babies. If you are female and having sex that could lead to pregnancy, you must agree not to become pregnant. Because of the risk involved, you must use at least one method of birth control that you discuss with the study staff. You must continue to use at least one method during the 24-weeks of study treatment and also for an additional 4 weeks after stopping study treatment. You may choose one of the birth control methods listed below:

- Condoms (male or female) with or without a spermicidal agent. Condoms are recommended because their appropriate use is the only contraception method effective for preventing HIV transmission
- Diaphragm or cervical cap with spermicide
- IUD
- Hormone-based contraceptive

If you can become pregnant, you must have a pregnancy test before you enter this study. The test must show that you are not pregnant. If you think you may be pregnant at any time during the study, tell your study staff right away. The study staff will talk to you about your choices. If you become pregnant while on the study you will be asked if you wish to continue in the study and come for study visits. You will also be asked if the study staff can contact you by phone once the pregnancy has ended to see how both you and the baby are doing. You will not receive any further study treatment that is scheduled. You will be asked to sign a pregnancy consent form.

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

Breastfeeding

It is unknown whether the study treatment passes through the breast-milk and may cause harm to your infant. You must not breast-feed if you are in this study.

Are There Benefits to Taking Part in This Study?

If you take part in this study, there may or may not be a direct benefit to you, but no guarantee can be made. The effect of chloroquine on HIV infection is unknown. Chloroquine might reduce helpful immune activity (the body's defense function) against the HIV virus, but it is possible that the study treatment will reduce more of the harmful activity than good immune activity. It is also possible that you may receive no benefit from being in this study. Information learned from this study may help others who have HIV.

What Other Choices Do I Have Besides This Study?

Instead of being in this study you have the choice of:

- treatment with prescription drugs available to you
- treatment with experimental drugs, if you qualify
- no treatment

Please talk to your doctor about these and other choices available to you. Your doctor will explain the risks and benefits of these choices.

What About Confidentiality?

We will do everything we can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have obtained a Certificate of Confidentiality from the U.S. Federal Government. This certificate means that researchers cannot be forced to tell people who are not connected with this study, such as the court system, about your participation. Also, any publication of this study will not use your name or identify you personally.

People who may review your records include the U.S. Food and Drug Administration, University of Pennsylvania IRB, National Institutes of Health (NIH), Office for Human Research Protections (OHRP), the ACTG, study staff, and study monitors. Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to yourself or others, we will be required to tell the proper authorities.

What Are the Costs To Me?

Taking part in this study may lead to added costs to you and your insurance company. In some cases it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

The study treatment (chloroquine/placebo) that you receive will be supplied by the study.

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

Will I Receive Any Payment?

You will be compensated according to the following schedule for your time and inconvenience to attend study visits:

Screening: \$5 visit; \$20 each for hearing and eye exam: \$45

Pre-entry: \$5

Enroll, wks 4, 10, 16, 22, 28 (off study): \$25

Weeks 12 and 24 (visit + eye exam): \$45.

Thus, if you attend all visits, the maximum compensation you will receive from the study is \$220.

Note that this is the only compensation you will receive from the study; there is no additional reimbursement for parking, public transportation or child care.

What Happens If I Am Injured?

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event that you are hurt or injured as a result of participation in this research study, please contact the investigator listed on page one of this form.

In the event of any physical injury resulting directly from research procedures, medical treatment will be provided by the University of Pennsylvania without cost to you. Financial compensation is not otherwise offered from the University of Pennsylvania or the National Institutes of Health. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

What Are My Rights As a Research Subject?

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. Your healthcare provider will treat you the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. If you want the results of the study, let the study staff know.

What Do I Do If I Have Questions Or Problems?

For questions about this study or a research-related injury, contact:

- Pablo Tebas, MD (215-349-8092)
- Clinical Trials Unit (215 349-8092)

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

A5258, Vsn 1.0, 12/17/08: Chloroquine for Reducing Immune Activation.

CONSENT

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

Name of Subject (Please Print) Signature of Subject Date

Name of Person Obtaining
Consent (Please Print) Signature Date