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MEDICAL RECORD

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

• Adult Patient or • Parent, for Minor Patient

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INSTITUTE: \_\_\_\_\_

STUDY NUMBER \_\_\_\_\_ PRINCIPAL INVESTIGATOR: Dr. Stephen E. Straus

STUDY TITLE: The Tolerance of HIV-infected Patients with Herpes Group or Hepatitis B

Virus Infections to Oral Doses of FIAU.

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### INTRODUCTION

We invite you (or your child) to take part in a research study at the National Institutes of Health. It is important that you read and understand several general principles that apply to all who take part in our studies: (a) taking part in the study is entirely voluntary; (b) personal benefit may not result from taking part in the study, but knowledge may be gained that will benefit others; (c) you may withdraw from the study at any time without penalty or loss of any benefits to which you are otherwise entitled. The nature of the study, the risks, inconveniences, discomforts, and other pertinent information about the study are discussed below. You are urged to discuss any questions you have about this study with the staff members who explain it to you.

People infected with the Human Immunodeficiency Virus (HIV) are at risk for complicating infections. Among these are infections with herpesviruses including herpes simplex virus, the varicella-zoster virus, the cytomegalovirus (CMV) as well as hepatitis B virus (HBV). Herpes simplex and varicella-zoster viruses are frequent causes of blistering and ulcerating skin sores in patients with HIV infection. CMV is capable of causing destruction of retina of the eye as well as serious infections of the brain, lungs, and other organs in patients with HIV infection. HBV can cause slowly progressive destruction and failure of the liver. As a person whose immune defenses have been weakened by HIV and who may have evidence of active infection with one or more of these viruses, you are invited to participate in a study of a new drug designated to control one or more of these infections and their potential serious consequences in people with impaired immune systems.

The present study is designed to determine how well patients like yourself can tolerate various doses of the antiviral drug FIAU. In the laboratory, FIAU is capable of blocking the growth of herpes simplex virus, varicella-zoster virus, CMV, and hepatitis B virus. Past experience with drugs closely related to FIAU suggests that we might be able to give patients oral doses of FIAU that are adequate to block the growth of these viruses while causing minimal side effects. To arrive at an answer as quickly as possible, this study is being conducted in conjunction with AIDS experts at three major universities. We will be starting patients at low doses of FIAU and gradually raising the dose with subsequent patients, until we find a level that may be capable of blocking growth of the viruses or until toxic side effects occur (see page 3), whichever comes first. Even if FIAU appears safe and capable of suppressing herpes group or hepatitis B virus infections, we cannot give more of it to you until the Food and Drug Administrations approves our doing so.

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PATIENT IDENTIFICATION

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

• Adult Patient or • Parent, for Minor Patient

MEDICAL RECORD

CONTINUATION SHEET for either:  
NIH 2514-1, Consent to Participate In A Clinical Research Study  
NIH 2514-2, Minor Patient's Assent to Participate In A Clinical Research Study

STUDY NUMBER: \_\_\_\_\_ CONTINUATION: page 2 of 6 pages.

### ELIGIBILITY

To be eligible for the study, you must be 13-65 years of age and have proven infection with HIV. You must be strong enough to carry on normal activities of daily living, have no significant kidney problem and be able to come to the clinic on your own for all the visits that the study requires. The immune status of all patients must be such that the total number of CD4-positive lymphocytes be greater than or equal to 200/mm<sup>3</sup>. If you are taking AZT, you are eligible for this study only if you have been receiving doses of 600mg/day or less for 6 weeks or more before starting FIAU. If you are not currently taking AZT, it cannot be started during the 2 week FIAU treatment. Both men and women participants must agree to use birth control for the entire 2-week study period, and 3 months thereafter, because FIAU, like its related antiviral drugs, could damage the ability of men and women to conceive or deliver normal babies. Women who participate in the study will undergo a pregnancy test within 2 weeks prior to starting FIAU.

Patients who have evidence of any other serious complications of HIV infection, or who are taking any other antiviral or immune-stimulating drug, cannot participate. You cannot be on acyclovir within 1 week of starting treatment and throughout the 2-week period of FIAU treatment. Aerosolized pentamidine treatment and other non-experimental medications may be continued.

You may be eligible for the study if you have active infections with herpes simplex virus, varicella-zoster virus, CMV, and/or hepatitis B virus. If you have active herpes simplex or varicella-zoster virus infections, you may receive FIAU only if your infections have proven unresponsive to acyclovir treatment. If you have CMV infection, you cannot receive FIAU if you have evidence that the virus is actively injuring the retina of your eye or other organs. Before starting treatment, an ophthalmologist will examine your eyes to be sure there are no signs of CMV infection. Patients who have chronic active hepatitis B virus infection can participate in this study only after a given FIAU dose level has proven to be well tolerated in individuals who are otherwise the same, but do not have chronic hepatitis.

### STUDY PROCEDURES

If you have been screened and found eligible for this study, FIAU will be dispensed to you from our NIH pharmacy as a liquid which you will mix in a glass of water to drink 3 times a day for 14 days. You will receive the same dose of FIAU for all 14 days. It must be taken at least 1 hour before or 3 hours after meals, so that food will not interfere with its absorption into the blood stream. You will need to come to the NIH pharmacy once a week to pick up your prescribed FIAU.

PATIENT IDENTIFICATION

CONTINUATION SHEET for either:

NIH-2514-1 (10-84)

NIH-2514-2 (10-84)

P.A. 09-25-0099

STUDY NUMBER: \_\_\_\_\_ CONTINUATION: page 3 of 6 pages.

On study day 1, you will be required to be in the clinic to take your first dose of FIAU, and to return 8 hours later, just before your second dose, so that we can draw blood to evaluate the levels of the drug in your blood stream at that time. You will then be asked to return to the clinic on days 2, 3, 5, 7, 10 and 14 following your first dose of FIAU, for examinations and repeated tests of blood, urine and stool. Your participation in this study ends after the 14th day unless you have chronic hepatitis B virus infection. If you have chronic hepatitis B virus infection, we will examine you briefly in clinic and obtain additional blood samples at days 21 (1 week post treatment) and 42 (4 weeks post treatment). Your participation in this study may also be ended should treatment side effects be too bothersome (see below), or if you fail to take the FIAU properly or keep many of the clinic appointments.

This study requires us to draw blood tests on every visit. The total amount of blood to be drawn will be less than 150cc (about 10 tablespoons). All blood samples will be drawn from a vein in your arm. Blood drawing hurts briefly, can occasionally lead to a local bruise, and rarely triggers fainting.

Also, we will have to test you stool for trace amounts of blood to determine if FIAU is causing bowel or stomach irritation. The stool samples can be provided by you or, if more convenient, may be taken by a brief rectal insertion with a gloved finger. There will be four such tests in the course of the study.

### TOXIC SIDE EFFECTS

FIAU is a new drug that has not previously been given to patients. However, it is very closely related to another drug that has been given by mouth and intravenously to well over 100 patients. That drug, known as FIAC, is rapidly broken down in people's bodies to FIAU, therefore, we think that the potential side effects should be virtually the same as those found with FIAC. Since FIAU is a new drug, all of its short or long term side effects are not yet known.

FIAC is known to cause some side effects when given intravenously or orally at doses that would produce FIAU concentrations in your blood equivalent to or many time higher than that achieved in the present study. For example, high doses of FIAC can cause a fall in the number of red blood cells (anemia). It is unlikely that the degree of anemia would be great at the dosage of FIAU you will be taking, but if you are also taking AZT, these side effects may be more severe and more blood transfusions may be required than would be necessary to treat anemia due to AZT alone. High doses of FIAC can also cause a fall in the number of white blood cells (leukopenia). Again, if you are on AZT this problem could become worse, such as to increase your risk of other complicating infections. Some infections that occur in people with very low white blood cell counts can be very serious, even fatal, but these are uncommon in people with HIV infections. Similarly, FIAC can lead to a decrease in platelets, the blood elements required for clotting.

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NIH 2514-1, Consent to Participate In A Clinical Research Study  
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STUDY NUMBER: \_\_\_\_\_ CONTINUATION: page 4 of 6 pages.

Throughout treatment with FIAU, the number of your red and white blood cells and platelets will be measured repeatedly. If we detect any clinically significant decreases in the cells or platelets, we may stop your FIAU treatment. Very high doses of FIAC also were associated with reversible lung congestion and neurologic problems like seizures. Certainly, if necessary, standard medical therapy of these complications will be provided and treatment can be stopped whenever needed or desired.

In some HIV infected patients treated with FIAC in another study, we noted that there was a rise in blood levels of a muscle enzyme called CPK. This is a chemical released into the blood stream any time there is a degree of inflammation and/or damage to muscles. One of the few individuals in whom this was observed had muscle aches, but the rest of the individuals were entirely unaware of the process. That individual also had some temporary kidney function abnormality and a hallucination. It was realized that only individuals with CD4 counts of less than 200/mm<sup>3</sup> had these side effects of FIAC. It is our hope that by selecting patients in this study such as yourself with CD4 counts of 200 or greater, we can avoid these side effects. Nonetheless, we will go to considerable lengths in this study to avoid any side effects of FIAU related to muscle. We urge all patients not to engage in strenuous physical activity during the time of treatment. Strenuous activity itself could raise blood CPK levels. We will be checking blood CPK levels during the study as well as doing a simple test of muscle strength in which we determine how long it takes an individual to rise ten times from a sitting position in an ordinary chair.

Based upon our experience with FIAC, it is possible that FIAU could cause stomach upset, nausea, or even vomiting. If needed, we will give you medications to try to control these side effects. If these medications fail to help you, we will stop the FIAU completely.

#### ALTERNATIVE TREATMENTS

There are alternative treatments to FIAU for some of the types of viral infection we are studying:

For HSV infection	The antiviral drug acyclovir is the standard treatment for active HSV infections. You have been chosen for FIAU treatment only because your HSV infection has failed to show an obvious clinical response to acyclovir pills. Alternative treatment to acyclovir pills would include admitting you to the hospital for intravenous acyclovir treatment or attempting to get another experimental drug for refractory HSV infections, a drug known as foscarnet. That drug is also given intravenously and has known side effects. Should you have active HSV infection, your oral acyclovir treatment would need to be stopped for 1 week prior to starting FIAU.
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PATIENT IDENTIFICATION

CONTINUATION SHEET for either:

NIH-2514-1 (10-84)

NIH-2514-2 (10-84)

P A 09-25-0099

STUDY NUMBER: \_\_\_\_\_ CONTINUATION: page 5 of 6 pages.

- Varicella-zoster virus - Should you have an active zoster infection, you will be eligible for FIAU treatment only if your infection has proven refractory to treatment with acyclovir pills. Alternative treatments include admitting you to the hospital for intravenous acyclovir or attempting to get another experimental intravenous medication known as foscarnet.
- CMV infections - Should you be chosen to be treated with FIAU for CMV infection, it would be done so with the understanding that you do not at the present time have evidence of an active CMV infection involving the eyes or other vital tissues. Should you have CMV infection of the retina or other tissues, you will not be eligible for this study. It is generally not considered necessary to treat the asymptomatic CMV infections in patients with HIV. We would choose to do so in you as an experimental test of the drug FIAU.
- HBV infection - There are no proven alternative therapies for chronic HBV infections in patients who are also infected with HIV. Patients who are not also infected with HIV have shown temporary or even permanent improvement of the HBV infection by long-term injections with the drug interferon. Prior to your considering this study, you will be counseled regarding your suitability for interferon treatment as an alternative to FIAU.

**POTENTIAL BENEFITS**

Besides helping us learn about treatments for viral infections in individuals with HIV, you may benefit from participating in this study in several regards. First, if you have otherwise refractory herpes simplex or zoster infection, that infection may improve during FIAU treatment. Second, it is conceivable that what we learn about FIAU may provide us simpler and more effective ways of treating CMV infections. Third, should you be treated for chronic HBV infection, we may identify a drug that could benefit your infection. Because FIAU has not been used previously, there is no way of determining whether any of these potential benefits are likely.

STUDY NUMBER

OTHER PERTINENT INFORMATION

1. **Confidentiality.** When results of a study such as this are reported in medical journals or at meetings, the identification of those taking part is withheld. Medical records of Clinical Center patients are maintained according to current legal requirements, and are made available for review, as required by the Food and Drug Administration or other authorized users, only under the guidelines established by the Federal Privacy Act.
2. **Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical care for any physical injury resulting from your participation in research here. Neither the Clinical Center nor the Federal government will provide long-term medical care or financial compensation for such injuries, except as may be provided through whatever remedies are normally available under law.
3. **Payments.** If you are a patient, you are not paid for taking part in NIH studies. Exceptions for volunteers will be guided by Clinical Center policies.
4. **Problems or Questions.** Should any problem or question arise with regard to this study, with regard to your rights as a participant in clinical research, or with regard to any research related injury, you should contact the principal investigator, **Stephen E. Straus, M.D.**, or these other staff members also involved in this study:  
**Barbara Savarese, R.N.**  
 Building 10 Room 11N113 Telephone: (301) 496-5221  
 National Institutes of Health  
 Bethesda, Maryland 20205

- a. **Consent Document.** It is suggested that you retain a copy of this document for your later reference and personal records.

COMPLETE APPROPRIATE ITEM BELOW, A or B:

**A. Adult Patient's Consent.**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

\_\_\_\_\_  
 Signature of Adult Patient & Date Signed

**B. Parent's Permission for Minor Patient.**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study  
 (Attach NIH 2514-2, Minor's Assent, if applicable.)

\_\_\_\_\_  
 Signature of Parent(s) & Date Signed

\_\_\_\_\_  
 (If other than parent, specify relationship)

\_\_\_\_\_  
 Signature of Investigator & Date Signed

\_\_\_\_\_  
 Signature of Witness & Date Signed

PII IDENTIFICATION

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