INSTITUTE: National Cancer Institute

STUDY NUMBER: 09-C-0037 PRINCIPAL INVESTIGATOR: Tito Fojo, M.D., Ph.D

STUDY TITLE: A Phase II Clinical Trial of Ixabepilone (Ixempra®, BMS–247550, NSC 710428), an Epothilone B Analog, in Cervical Cancer

Continuing Review Approved by the IRB on 04/09/12
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INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

DESCRIPTION OF RESEARCH STUDY

This is a Phase II study for the experimental treatment of cervical cancer. A Phase II study is one that begins the process of examining whether a specific drug might be useful in a particular type of cancer. It follows Phase I studies that are conducted to determine the amount of a drug that can be safely administered. The drug to be examined in this study is ixabepilone. The purpose of this Phase II study is to determine whether ixabepilone administered every day for five consecutive days is effective in the treatment of cervical cancer. To determine if ixabepilone is effective in the treatment of cervial cancer, up to 76 patients will be enrolled in this study. Ixabepilone is a member of the epothilone class of drugs. The epothilones are drugs

that interfere with the ability of cancer cells to divide. In the way they kill cells, they are very similar to a class of compounds known as the taxanes. The taxane class of drugs include the drug taxol. Taxol has been used extensively in a wide variety of cancers and is effective in the treatment of several forms of cancer, including cancer of the breast, cancer of the ovary and cancer of the lung. The epothilones are similar to taxol, but also have other characteristics that may make them better. The latter include the ability to work in cells that are resistant to taxol.

You will be expected to stay in the area for about 7 to 8 days in the first treatment cycle. In subsequent cycles you will need to be in the area for the five days during which the drug is administered. The amount of drug you receive in the first cycle will be that administered to all patients. In subsequent cycles the dose may be adjusted according to how well your body responds to the chemotherapy. The dose will not be increased, but it may be decreased, if necessary. Each cycle lasts 21 days. The first 5 days of a cycle are the days you receive ixabepilone and the next 16 days are the rest period before the next cycle begins. During the 16 day rest period you will return to your home. You will need to have your blood tested at home twice a week during the first two cycles and then once a week during later cycles. The results of these blood tests will be sent to us to help monitor your safety.

Ixabepilone will be administered by vein. Ixabepilone will be administered over a 60-minute period, every day for 5 days in a row. The number of cycles of experimental therapy you receive will depend on your clinical situation. We plan to use x-rays (CT scans) and other studies if necessary, to determine if your tumor is responding to the treatment. The CT before the first cycle will be the 'baseline CT'. CTs will be done following cycle 2, cycle 4 etc and compared to the baseline CT as well as the previous CT. In making decisions as to whether to continue treatment we will be guided by information from the CT and other studies as well, as the physical examination and reports from you on how you are tolerating the treatment. The experimental therapy will be stopped if you have worsening of your disease or significant toxicity.

During cycle one tumor biopsies will be obtained on two separate days, if you are willing and able to undergo a biopsy procedure. The first biopsy will be obtained prior to the first dose of ixabepilone. This can happen during the day(s) before ixabepilone begins, or the morning of the first dose. The second biopsy will be obtained either on the 4^{th} or 5^{th} day of ixabepilone, after you have received the infusion that day. The purpose of these biopsies is to analyze structures within the tumor cells for evidence that the chemotherapy is penetrating the tumor and causing disruption to its structure. One specimen will be of the tumor without chemotherapy and the other will be of the tumor with chemotherapy. These biopsies are optional. You can still be treated on this study, even if you refuse the biopsies. They will not benefit you, but will help our research. The following section explains the procedure for obtaining biopsies.
A physician may perform simple biopsies in an examining room using local anesthesia. Other biopsies will be performed in the radiology suite with the help of special equipment such as a CT

scan or an ultrasound. These will be performed under local anesthesia by an experienced radiologist. A needle will be used to obtain the tumor sample. It will pass through your skin and some of the internal tissues between the surface of your skin and the tumor. We will use this tissue sample to examine some of the proteins that are important in how cancer cells react to drugs such as ixabepilone. Part of this sample will be saved and may be used for additional investigations at the conclusion of the study. We want to emphasize that the biopsy will be performed exclusively for research purposes. You will not derive any personal benefit from this. We would also emphasize that we consider it an important part of the study, because we hope it will help us understand why the drug works, if it does, or why it did not work against the cancer if it does not. Furthermore, the results of tissue (specimen) bank research may help find new ways to learn about, prevent, or treat cancer and other diseases. In the following section you will be asked if you would be willing have these biopsies done for research. Even if you sign "yes" to the biopsies you can change your mind later and not have the biopsies.

It will also be necessary to draw a small amount of blood five times during the first cycle of chemotherapy. These blood draws will coincide with the biopsies, if you have biopsies. If you do not have biopsies, the blood tests will not be done. This will allow us to see how your body is handling ixabepilone. Less than two teaspoons of blood will be drawn for each sample. The blood samples will be collected on Day One, prior to the ixabepilone drug infusion and then at 1, 8 and 24 hours after the drug is given. An additional blood sample will be collected within 1 hour of the biopsy on either Day 4 or Day 5.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

1. I agree to have the two tumor biopsies for the research tests as specified in this study.

Yes No Initials_____

2. I also agree to have the five blood samples collected at the time of the biopsies.

Yes No Initials_____

Optional Studies

We would like to keep some of the specimens and data that are collected for **future research**. These specimens and data will be identified by a number and not your name. The use of your specimens and data will be for research purposes only and will not benefit you. It is also possible that the stored specimens and/or data may never be used. Results of research done on your specimens and/or data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you decide now that specimens and data can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and data. Then specimens that remain will be destroyed and your data will not be used for future research.

3. My specimens and data may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Initials_____

4. My specimens and data may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials_____

5. Someone may contact me in the future to ask permission to use my specimens and/or data in new research not included in this consent.

Yes No Initials_____

If your tumor grows while you are being treated with ixabepilone, your experimental treatment will be stopped. In addition, your doctor can stop treatment at any time if in his/her opinion your continued participation would be detrimental to your health or the side effects are unmanageable. You may decide to stop the experimental treatment and withdraw from the study at any time. Upon completion of this study, you may be given the option of participating in additional research protocols that may be appropriate for you, if such protocols exist. If they do not, you will be returned to the care of your referring physician.

Your tumor may shrink or become undetectable by the CT scans. If this were to happen, you would continue to receive ixabepilone for several more cycles until the physicians agree you have achieved the best response possible. At that time, you would stop receiving ixabepilone, but continue to be monitored by us. You will continue to have CT scans and physical exams every 6 weeks, then possibly extending to every 3 to 4 months. You may have these visits done here at the NIH Clinical Center, or at your local physician's office. If you have scans done at your local office, we will request a copy of the scan and physician's notes for your records here in the trial.

ALTERNATIVE APPROACHES OR TREATMENTS

It is important to stress that participation in this protocol does not constitute promise of long-term care here at the NIH Clinical Center.

If there is no research study that is suitable for you and your state of disease, you will be returned to the care of your referring doctor or institution or to alternate sources of care closer to home.

It is conceivable that participation in this study may make you ineligible to participate in certain other research protocols because the requirements for entry into these protocols may disallow patients who have been on certain drugs.

You may decide now not to receive treatment in this protocol or you may choose at any point in time to stop the drug and withdraw from the protocol; in either case you would be returned to the care of you referring physician.

Because of the type and extent of your tumor, chemotherapy is an option other than surgery or radiation.

Alternative approaches that could be used may include:

1. Radiation treatment that sometimes can control tumor growth in local areas such as lymph nodes, bones, lung and bowel. However, this approach will not effectively treat disease that has spread beyond small areas, as in your case.

2. Surgery that can be used to remove disease from local areas such as lymph nodes, lung and bowel but is not useful for long term control when the disease has spread.

3. Another option is
   - Getting no treatment.
   - Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

4. FDA-approved chemotherapy or drug treatment.

5. Other experimental therapies.

RISKS OR DISCOMFORTS OF PARTICIPATION

Local anesthesia will be used when biopsies of tumor masses are performed. The risks associated with these procedures are pain, bleeding and local infection. These risks will be individually explained to you at the time of the procedure. We would also emphasize that if we are unsuccessful in our attempts to obtain a sample of your tumor, you will not be disqualified from participating in the study. That is to say, if we feel that you are eligible for the study, and that a sample of tumor can be obtained without surgery, you will be eligible to enroll on study even if we are not successful in our attempt to obtain a sample of your tumor.

If biopsies are performed, they will be obtained for experimental purposes including performance of tests on your tumor that may help us understand why it responds or does not respond to treatment. As indicated above, biopsies requiring major surgery (opening the chest or abdomen), or those requiring general anesthesia will only be obtained if necessary for your medical care and will not be obtained for experimental purposes. It is important for you to understand that the biopsies of tumor will be performed for experimental purposes, so that we can try to determine why tumors become resistant to chemotherapy. You will not derive any personal benefit from these biopsies.

This research study involves exposure to radiation from up to 2 CT-directed biopsies. This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 0.26 rem which is below the guideline of 5 rem (or 0.5 rem in children) per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.
If you are pregnant you will not be permitted to participate in this research study. If you are breast feeding and the protocol involves injection of radioactive material you will not be permitted to participate. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

Blood samples will be obtained at five time points during cycle one. A heparin-lock device may be placed during this time to prevent repeated use of needles. This is placement of a temporary needle in your arm and using heparin in small amounts to prevent blood from clotting in the needle. Alternately if you have a device that has been inserted to allow access to your veins (a central venous catheter), such as a 'port' or 'picc', blood can be drawn from these devices. Since chemotherapy will result in decreased ability to make new red blood cells, the drawing of blood may increase the risk of anemia and the need for a blood transfusion, or treatment with a drug to increase your red blood cell count.

To receive this experimental therapy you can have a central venous catheter placed. This is a catheter that is placed under the skin of your chest, neck or arm and enters a major vein. This catheter is used for administration of chemotherapy and drawing of blood. These catheters are called 'ports' or 'piccs'. A surgeon in the operating room using local anesthesia inserts the port catheter. Piccs are inserted by specially trained nurses in our procedure area. The risks associated with these procedures include pain, bleeding, infection, and development of air in the chest. Air in the chest outside the lung would require temporary placement of a chest tube by the surgeon. Other risks of the catheter include infection and clotting of your veins, which could require removal of the catheter for treatment. These risks will be explained to you in more detail at the time of insertion.

The purpose of this phase II study is to determine whether ixabepilone is effective against cervical cancer. Ixabepilone is approved by the Food and Drug Administration (FDA) for the treatment of metastatic breast cancer. Although it is an approved drug, we are still studying ixabepilone to see if it might be useful in other cancers beside breast cancer. For this reason, the study is considered experimental, because we do not know if ixabepilone will be effective against cervical cancer.

All patients enrolled in the current study will be observed carefully for the development of any side effects and these will be recorded. Blood tests will be monitored frequently and you will also undergo periodic physical examinations, and be asked to report any side effects you might have experienced. Should any side effects other than those listed here become apparent during the course of the study, you will be advised of these at the time of study entry, or at any time during the course of the study. **We would also caution you not to take St. John's Wort while receiving ixabepilone**, since this may lead to a drug interaction that could be serious. You will need to report all prescription, over-the-counter medicines, and herbal remedies to the study team so we can review them for potential drug interactions. This includes medicines and herbs taken in the month before you begin the study and also any new medicines or herbs you would like to start during the study. Your study team must review the medicines and herbs before you begin to take them.

Anticipated side effects from Ixabepilone may include but are not limited to the following:

Likely:

- Lack of enough red blood cells (anemia)
- Diarrhea
- Nausea or the urge to vomit
- Vomiting
- Fatigue or tiredness
- Increased blood level of a liver or bone enzyme (alkaline phosphatase)
- Decreased number of a type of white blood cell (neutrophil/granulocyte)
- Decreased number of a type of blood cell that help to clot blood (platelet)
- Decrease in the total number of white blood cells (leukocytes)
- Muscle pain
- Inflammation (swelling and redness) or degeneration of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning
- Hair loss

Less Likely:

- Fever associated with dangerously low levels of a type of white blood cell (neutrophils)
- Abnormally fast irregular heartbeat involving the upper chambers of the heart (atria)
- Abnormally fast regular heartbeat involving the upper chambers of the heart (atria)
- Period of very rapid and regular heartbeats that begins and ends suddenly
- Slow heartbeat; regular rhythm
- Fast heartbeat; regular rhythm
- Fast heartbeat usually originating in an area located above the ventricles
- Excessive tearing in the eyes
- Belly pain
- Irritation or sores in the lining of the anus
- Constipation
- Irritation or sores in the lining of the mouth
- Irritation or sores in the lining of the rectum
- Irritation or sores in the lining of the small bowel
- Fever
- Pain
- Abnormal reaction of the body to substances, called allergens, that are contacted through the skin, inhaled into the lungs, swallowed, or injected (allergic reaction)
- Infection
- Inflammation (swelling and redness) of the skin caused by drugs after radiation therapy

- Increased blood level of a liver enzyme (ALT/SGPT)
- Increased blood level of a liver enzyme (AST/SGOT)
- Increased blood level of a liver pigment (bilirubin) often a sign of liver problems
- Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)
- Increased INR (measure of the ability of the blood to clot properly) which increases the risk of bleeding
- Loss of appetite
- Dehydration (when your body does not have as much water and fluid as it should)
- Joint pain
- Muscle weakness of the whole body
- Leg and/or arm pain
- Pain in the area of the tumor
- Dizziness (or sensation of lightheadedness, unsteadiness, giddiness, spinning or rocking)
- Taste changes
- Speech problems
- Headache or head pain
- Nerve pain
- Weakness or paralysis (loss of muscle function) caused by damage to peripheral nerves (those nerves outside of brain and spinal cord)
- Fainting
- Difficulty sleeping or falling asleep
- Difficulty emptying the bladder
- Cough
- Shortness of breath
- Hiccups
- Decrease in the oxygen supply to a tissue
- Irritation or sores in the lining of the voice box
- Irritation or sores in the lining of the throat
- Inflammation (swelling and redness) of the lungs
- Irritation or sores in the lining of the windpipe
- Loss of some or all of the finger or toenails
- Itching
- Skin rash with the presence of macules (flat discolored area) and papules (raised bump)
- Sudden reddening of the face and/or neck
- Low blood pressure

Rare but Serious:

- Partial or complete blockage of the small and/or large bowel. Ileus is a functional rather than actual blockage of the bowel.
- Build up of a large amount of fluid between the layers of tissue that line the lungs and chest cavity
- Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue
- Swelling and redness of the skin on the palms of the hands and soles of the feet
- Increase in the number and size of the pores in the capillaries (small blood vessels) which causes leakage of fluid from the blood to the tissue spaces, resulting in dangerously low blood pressure, swelling and multiple organ failure
- Ixabepilone is dissolved in a solution that contains a compound called cremophor EL. Because some patients have had allergic reactions to the cremophor EL, you will receive two medications prior to the administration of ixabepilone, in order to prevent an allergic reaction. The two medications will be diphenhydramine (Benadryl) and ranitidine (Zantac). Although the likelihood a serious side effect will occur from receiving these drugs is low, you should be aware they have potential side effects. Despite receiving premedications, you may still develop an allergic reaction. If that happens the infusion will be stopped and additional diphenhydramine, ranitidine and a third medication, dexamethasone (Decadron), may be added to treat the reaction. This is a rare occurrence.

If you have received prior radiation therapy, you may experience cystitis or obstruction of the bladder after receiving ixabepilone. Cystitis is an inflammation of bladder. It may cause pain when trying to urinate. The wall of the bladder may become thicker causing the opening of the bladder to become narrower, making it more difficult to urinate. If you experience any of these changes please notify your study team immediately.

1. For diphenhydramine (Benadryl), these include sedation, sleepiness, dizziness, difficulty with coordination, abdominal pain, dry mouth, flushing, and temporary difficulties passing urine. Diphenhydramine may impair your ability to drive and you may need to seek transportation to and from clinic visits.

2. For ranitidine (Zantac) potential side effects you may experience include headache, fatigue, dizziness, mild diarrhea, temporary confusion and a rash.

3. For dexamethasone (Decadron) potential side effects you may experience include increased susceptibility to infection, lower values of calcium, potassium, sodium in your blood, high blood pressure and change in mood. This medication would only be given for a few days during a cycle.

4. Finally, there is evidence that some drugs that you may be taking for other reasons may affect the ability of your body to eliminate ixabepilone. If you are taking any of these drugs the investigators will discuss the options available including substituting other similar drugs or withholding their administration for a defined period.
   These drugs include the following: ketoconazole, itraconazole, clarithromycin, atazanavir, nefazodone, saquinavir, telithromycin, ritonavir, amprenavir, indinavir, nelfinavir, delavirdine, voriconazole, and St. John's Wort. Please discuss all medications and herbs with your study team prior to taking them.

5. You should not drink grapefruit juice while on this study, because it can interact with other medications.

Pregnancy

Patients with childbearing potential should use adequate birth control measures while on study, and for two months after discontinuing therapy. Pregnant and breast-feeding patients will not be allowed on study due to the experimental nature of the protocol and the possibility of jeopardizing the health of the child. If you or partner become pregnant while on study contact your NIH doctors immediately.

POTENTIAL BENEFITS OF PARTICIPATION

This is an experimental study. While we hope this will be of some benefit to you, it is impossible to predict whether ixabepilone will be effective against cervical cancer. It is also impossible to predict any side effects with certainty.

RESEARCH SUBJECT'S RIGHTS

Any complication arising from this treatment will receive full and prompt medical attention. However, neither the National Cancer Institute, the Federal Government, nor the Clinical Center, can provide financial compensation for injury or long-term medical treatment for such injuries, except as may be provided through whatever remedies are normally available under law. Any significant new findings that relate to your treatment will be discussed with you.

PAYMENT

You will not be paid for taking part in this study. Your medical care and the costs of the laboratory and radiographic studies done at the Clinical Center, NIH will be at no expense to you. If the blood tests needed to monitor the effects of treatment are to be done by your local physician, you can be reimbursed for the costs if your insurance does not cover this expense; your NIH physician must obtain permission for this in advance. The NIH cannot, however, reimburse you for the costs of other types of medical care delivered outside the NIH, even if you

are seeking medical attention as a result of side effects from treatment given here, unless permission for this is secured in advance by your NIH physician. Similarly, we do not ordinarily reimburse the costs of diagnostic radiology tests (such as CT scans, MRI, or chest X-rays) done outside the NIH, even if they are done for the purpose of this study. The upper limit of reimbursement is $5,000 per patient.

What Happens after This Treatment is completed?

This depends on how you have responded to the experimental therapy. If all evidence of disease has disappeared, we will schedule periodic visits to the Clinical Center for follow-up examination and tests. If the disease does not disappear entirely or if it should recur after having disappeared for a period of time, then you may need further therapy. At that time you will be given the opportunity of participating in additional research protocols that may be appropriate for you. If no such protocols are available, you will be returned to the care of your local physician. It is important to stress that participation in this protocol does not constitute a promise of long-term medical care here at the Clinical Center. If there is no research study that is suitable for you and your stage of disease, you will be returned to the care of your private doctor or to a clinic in your local community. It is conceivable that participation in this study may make you ineligible to participate in certain other research protocols because the requirements for entry onto these protocols may disallow patients who have already been treated with certain drugs or who have had certain side effects from previous treatment. You may decide now not to receive treatment on this protocol, or you may choose at any point in time to stop the treatment and withdraw from the protocol; in either case you will be returned to the care of your referring physician.

COMMUNICATION

The NCI physicians involved in your case are available to answer all of your questions concerning this protocol. If you have any concerns or questions, you may contact Dr. Tito Fojo, the Principal Investigator (301-402-1357), and/or Maureen Edgerly, R.N., the Research Nurse at 301-435-5604. The NIH patient's rights representative (301-496-2626) will be available to answer questions you may have concerning your involvement in this study or your rights as a research subject. Officials of the Food and Drug Administration, the NCI, and the drug manufacturer (Bristol Myers Squibb) may review your patient records during this study, confidentially. A copy of this informed consent is on file with Institutional Review Board of the National Cancer Institute and a copy is available to you when you sign it and at any further time. Your participation in this protocol is entirely voluntary and you may refuse to participate or withdraw from this protocol at any time.

OTHER PERTINENT INFORMATION

1. **Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

   The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. **Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. **Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. **Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Tito Fojo, M.D.; Bldg 10, Rm 12N226, 10 Center Drive, Bethesda, MD 20892; Telephone: 301-402-1357. Other researchers you may call are: Maureen Edgerly, R.N., Telephone: 301-435-5604. If you have any questions about the use of your specimens and data for future research studies, please contact the Office of the Clinical Director, Telephone: 301-496-4251.

   You may also call the Clinical Center Patient Representative at 301-496-2626.

5. **Consent Document.** Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

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/ Legal Representative Date

_____
Print Name

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)/ Guardian Date

_____
Print Name

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

_____ _____ _____
Signature of Parent(s)/Guardian Date Print Name

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM APRIL 9, 2012 THROUGH APRIL 8, 2013.

_____ _____ _____ _____
Signature of Investigator Date Signature of Witness Date

_____ _____
Print Name Print Name