INSTITUTE: National Cancer Institute

STUDY NUMBER: 08-C-0078 PRINCIPAL INVESTIGATOR: Phillip A. Dennis, M.D., Ph.D.

STUDY TITLE: A Phase II trial of Pemetrexed (Alimta [Registered Trademark]) Combined with Sirolimus (Rapamycin, Rapamune [Registered Trademark]) in Subjects with Relapsed or Refractory NSCLC

Continuing Review Approved by the IRB on 04/9/12
Amendment Approved by the IRB on 03/27/12 (J) Date Posted to Web: 04/25/12
Consent for Phase II

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.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have a cancer that has relapsed following or failed to respond to standard therapy. Your current disease state must be one for which there is no known curative therapy. There may be other chemotherapeutic agents that could be used to treat your cancer.

Why is this study being done?
This is a research study looking at a new combination of drugs to treat non-small cell lung cancer, abbreviated NSCLC. You are being considered for this study because you have lung cancer that has not responded to standard treatments, recurred after standard treatments, has spread outside your lungs to other parts of the body and you have declined the standard therapies that were offered to you, or there are no other standard treatments available.

The purpose of this study is to test the safety and ability of study subjects to tolerate the combination of an experimental cancer drug, sirolimus (sih-ROLL-ah-mus), with another drug that is already used to treat lung cancer called pemetrexed (peh-meh-TREKS-ed). The major goal of this study is to figure out the ability of the two drugs to fight your cancer.

Pemetrexed is a drug that is already used to treat non-small cell lung cancer that does not respond to standard therapies or returned after treatment with standard therapies. Very few people (9 in 100) will respond to pemetrexed. Sirolimus is a drug that was originally designed to prevent organ rejection after transplant. Research shows it blocks a protein in our cells called mTOR. mTOR in normal cells is active when cells need to grow and then inactive when growth is completed. In cancer cells mTOR is active even when it should not be, which allows cancer cells to continuously increase in number. mTOR has been found to be unusually active in many cases of non-small cell lung cancer. Many studies done with cancer cells grown on plastic or in mice show that sirolimus can block the cancer cell's ability to grow by blocking mTOR. Although sirolimus is experimental in cancer patients, it has been used in humans in combination with other drugs to prevent rejection of organ transplants. A drug similar to sirolimus, temsirolimus, is approved for people with kidney cancer. Research also shows that by blocking mTOR, the cancer cell might also be more likely to respond to typical chemotherapy drugs. We are trying to increase the effectiveness of pemetrexed by combining it with sirolimus.

What do I need to tell my doctor before, during, and after this study?
It is very important that you tell your doctor all of the prescription as well as over the counter medications and herbal supplements you are taking before you start the study. **Do not start taking any medicine, hormone, vitamin, or herbal supplement once you are on the study until you have talked to your study doctor.** This is because some medicines or herbal supplements interfere with the breakdown of SIROLIMUS, making it either less effective in fighting your cancer or more toxic to you depending upon whether the breakdown is sped up or slowed down. Examples of these drugs include certain antibiotics, cholesterol lowering drugs, anti-seizure medication, some heart and high blood pressure medicines, and certain sedative, hormones, and herbal supplements. We will provide you with a handout that lists most of the drugs to avoid.

We will also want to know if you take non-steroidal anti-inflammatory agents (NSAIDS), such as ibuprofen, naproxyn, or celocoxib. The NSAIDS may prevent your kidneys from clearing the pemetrexed. We will ask you to stop taking NSAIDS for 5 days before you receive pemetrexed, the day of pemetrexed, and for two days after you receive pemetrexed.

If you choose to participate, you must use a form of contraception other than hormones (birth control pills, patches, vaginal rings) during this study and for 12 weeks after stopping the sirolimus. Hormones interfere with the breakdown of sirolimus. Your study doctor or regular doctor can help you choose another method of birth control to use while you are on the study.

Do not eat grapefruit, drink grapefruit juice or consume any grapefruit-containing products while you are on the study because it can also interfere with the breakdown of sirolimus.

What will happen if I take part in this research study?

Before I begin the study …
The following exams, tests or procedures will be done to find out if you can be in the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

Medical history: to learn about medical problems other than the cancer, your previous treatments for the cancer, and any problems you are currently having.

Blood tests: measure how liver, kidneys and blood clotting work, measure white blood cells, red blood cells and platelets, your blood sugar and blood salts, as well as your cholesterol and triglycerides levels, urine analysis, vitamin B12 and folate levels. To better understand the effects of sirolimus on your immune system we perform a blood test called lymphocyte subsets. This test measures the numbers of the various types of immune cells in your blood.

If you are a woman who is capable of becoming pregnant, we will do a blood test to be sure you are not pregnant.

CT Scans (or similar imaging test) to see where your cancer may be located.

EKG (a tracing of the electrical activity of the heart) is also performed.

If your cancer is easily sampled or biopsied, we may ask your permission for a biopsy. You may refuse to have the biopsy performed and still participate in the study. We will not ask you about the biopsy if the procedure is dangerous to you. The biopsy will tell us if the mTOR in your tumor is active The biopsy will be considered if your tumor is easy to reach by bronchoscopy or can be done by needle biopsy. Bronchoscopy is done by a lung specialist. A flexible tube is passed through your nose or mouth into your windpipe and then into your lungs. There is a light, camera, and tiny scissors on the end of the bronchoscope so the doctor can find areas that appear to have tumor and then take a small biopsy. You are given medicine during the bronchoscopy so that you do not experience discomfort. It is possible that you had this procedure to diagnose your lung cancer. Needle biopsies are done by a special radiologist. If the tumor is easy to reach, he will simply insert the needle into the mass after giving you numbing medicine. If the tumor is hard to see, he may use CT or ultrasound to help locate the tumor.

If we do not perform a biopsy we will ask you to provide some slides from time your cancer was diagnosed. This would be obtained from the pathology department where you had your original cancer diagnosis. You may participate in the study even if you do not want to obtain your slides or your slides are not available.

During the study
If the initial exams, tests, and procedures show that you can participate in the study, the following tests and procedures will be done during the study. The study is divided up into treatment cycles. The first cycle is 28 days long and the rest are 21 days long. The first day of each cycle is called day 1. Cycle 1 is the busiest cycle in terms of studies and tests and includes the following:

Study Day	What you will do
Day 1 Cycle 1	History and physical exam Blood and urine tests PET CT scan (explanation below) Start daily folic acid vitamin pill to prevent side effects from pemetrexed B12 injection to prevent side effects from pemetrexed Research blood tests to check for active mTOR Pregnancy test if appropriate Start daily sirolimus
Day 7 Cycle 1	Start dexamethasone for 3 days to prevent side effects from pemetrexed
Day 8 Cycle 1	History and physical exam Blood tests Research blood tests to check for active mTOR Get first dose of pemetrexed Continue dexamethasone
Day 9 cycle 1	Finish dexamethasone
Day 15 Cycle 1	History and physical exam Blood tests Blood test for sirolimus level
Day 22 Cycle 1	History and physical exam Blood tests Blood test for sirolimus
Day 28 Cycle 1	Start dexamethasone for 3 days
Day 1 Cycle 2 and Day 1 all future cycles	History and physical exam Blood, pregnancy tests Continue daily folic acid Get pemetrexed Blood test for sirolimus level

	Continue dexamethasone
Day 2 Cycle 2 & Day 2 all future cycles	Finish dexamethasone
Day 21 Cycle 2 & Day 21 all future cycles	Start Dexamethasone for 3 days
At the end of every 2 cycles	Follow up CT scan or MRI Follow up PET CT (if baseline was positive)-End of Cycle 2 only Repeat biopsy (if baseline biopsy was taken)-Optional Research Blood tests to check for active mTOR
At the end of every 3 cycles	B12 injection to prevent side effects of pemetrexed

A PET CT scan will be performed prior to starting treatment. The PET CT scan is a nuclear medicine scan. You are given a dose of radioactive sugar after you have not had anything to eat or drink overnight. A camera will measure radioactivity in various parts of your body. A CT scan is performed right after the camera measures radioactivity. Sugar is needed by cancer cells to grow, so the radioactive sugar is used by the cancer cells. Any part of your body in which the cancer is growing appears dark on the film. The darkness is given a number called SUV. The higher the SUV, the more likely that area represents a site of your cancer. The CT scan is matched up with the PET to see if the areas of uptake or blackness on the PET match tumor masses seen on CT. If your PET CT scan is positive, we will ask you to repeat the scan later in the study. If it was negative, then we will not repeat it later. If you have diabetes and your blood sugar measured after fasting overnight is elevated, the PET CT may not be done.

After cycle 1 we will only need to see you on the first day of each cycle unless you have problems. If so, we will see you at least once a week until your symptoms resolve. Your study doctor will determine what tests need to be done to follow your side effects and ensure a safe recovery.

Risks or Discomforts of Participation

What sort of side effects, discomfort, or inconveniences can I expect if I participate?

Everyone on the study will be carefully watched for side effects. Doctors don't know all of the side effects that may occur so it is important to report any changes you notice, even if your team does not ask specifically about them. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away with medicines and others go away soon after you stop treatment. In some cases, side effects can be serious, long lasting, or may never go away.

The side effects of sirolimus and pemetrexed given together are unknown. The side effects reported for sirolimus come from organ transplant patients. Transplant patients receive sirolimus along with other drugs that suppress the immune system. Therefore, it is difficult to know if sirolimus cause these same side effects in our study because subjects will not receive immune suppressing drugs.

In one cancer study, temsirolimus, a drug that is very similar to sirolimus, has been used along with a chemotherapy drug that is similar to pemetrexed. In that study there were serious side effects noted: Inflammation of the lining of the mouth with mouth sores making it difficult to eat and drink, diarrhea, nausea, vomiting, weakness, rash, low red blood cells, elevated blood sugar, fever while white blood cells are low, increasing the risk for infection, and low platelet count increasing risk for bleeding. There were also two instances of perforation of the intestine, or a hole

forming in the wall of the intestine, allowing stool to spill into the abdominal cavity, causing severe infection. The investigators thought the perforations were due to the combination drug therapy, and not the cancer. Because of the toxicity reported in this one clinical trial, we are starting at doses below what the Food and Drug Administration says is safe for each drug alone. The combination of pemetrexed and sirolimus may cause a rise of liver enzymes in your bloodstream, which may be a sign of damage to the liver.

Listed below are risks and side effects reported for **sirolimus** when given in combination with cyclosporine and corticosteroids (immune suppressing drugs) to patients who have received an organ transplant:

Occur in ≥ 20% of patients		Rare, but possibly life threatening
Weakness	Swelling	In liver transplant patients, fatal blood clots
Weight loss	Elevated cholesterol	In lung transplant patients, bleeding into airways
Weight gain	Elevated triglycerides	In transplant patients, increased risk of lymphoma
Fever	Low potassium	
Chest pain	Low phosphorous	
Headache	Pain in joints	
Pain	Insomnia	
High blood pressure	Tremor	
Constipation	Shortness of breath	
Diarrhea	Sore throat	
Upset stomach	Upper respiratory infection	
Indigestion	Inflammation in the lungs	
Nausea	Acne	
Vomiting	Urinary tract infection	
Abdominal pain	Low albumin	
Low red blood cells	Elevated glucose	
Low platelets	Low oxygen	
Low white blood cells		
Decreased kidney function		

The side effects of **pemetrexed** are listed below: These side effects were observed in 5% or more of patients receiving pemetrexed alone. These patients also took vitamin B12, folic acid and dexamethasone just as you will.

Occur in ≥ 5 % of patients These patients took Vitamin B12, folate, and dexamethasone	
Fatigue	Nausea
Fever	Vomiting
Edema	Abdominal pain
Loss of appetite	Sore muscles
Nausea	Infections
Constipation	Numbness in finger tips, toes, hands, feet
Chest pain	Shortness of breath
Ulcers in the mouth	Skin rash
Sore throat	Peeling of the skin after a skin rash
Low red blood cells	
Low white blood cells	
Low platelets	

Dexamethasone
Possible side effects include feeling unusually happy, great mood or other mood changes, headache, insomnia, edema, high blood pressure, flushing, high blood sugar, flatulence, and acne, may be observed with dexamethasone given intermittently as in this protocol. Other side effects associated with longer administration of dexamethasone include adrenal insufficiency (associated with low blood pressure and severe weakness), muscle weakness, Cushingoid state (high blood pressure, high blood sugar, weight gain in the stomach area, and loss of muscle in the arms and legs), and thinning of the bones making them prone to fracture. This medicine should be taken with food to avoid upset stomach.

Folic acid:
Side effects from folic acid are not common. Allergic reaction with rash, itching, swelling, dizziness, and trouble breathing have all been reported.

Vitamin B12 (Cyanocobalamin):
Side effects are rare but the following have been reported: Itching, rash, temporary rash that comes and goes and hives, itchy red swelling, diarrhea, and blood clot in legs have been reported. There may also be pain or redness associated with the injection.

BIOPSY
This research study may also involve exposure to radiation from a CT directed needle biopsy of your tumor. This radiation is not necessary for your medical care and it is for research purposes only. You do not have to undergo a tumor biopsy to participate in the study, and even if you do agree, the biopsy will not necessarily require the use of the CT scan. Your doctors will tell you how the biopsy will be done. If you agree to a CT directed biopsy, you will receive an additional 0.1 rem for each biopsy procedure. If you have 2 PET CT scans and 2 CT directed needle biopsies, you will receive an effective radiation dose of 3.9 rem.

For comparison, the average person in the United States receives a radiation exposure of 0.3 rem (or 300 mrem) per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from this research study is about the same amount you would normally receive in 12.2 years from these natural sources. If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, *An Introduction to Radiation for NIH Research Subjects*.

One possible effect that could occur at these doses is a slight increase in the risk of cancer. Please be aware that the natural chance of a person getting a fatal cancer during his/her lifetime is about 1 out of 4 (or 25 percent). The increase in the chance of getting a fatal cancer, as a result of the radiation exposure received from this research study, is 0.15%. Therefore, the total risk of fatal cancer may be estimated to increase from 25 percent to 25.15%. This change in risk is small and cannot be measured directly. Compared with other everyday risks, such as flying in an airplane or driving a car, this increase is considered slight.

Please tell your study doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Examples of scans to mention are 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 or breast feeding, you cannot participate in this research study. It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults.

Reproductive risks:
You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breast feed a baby while on this study. If you are of childbearing age, it is important you understand that you need to use barrier methods of birth control while on this study and for 12 weeks after stopping the sirolimus. Hormonal methods of birth control are **not** approved for use in this study. Please check with your study doctor about appropriate methods of birth control that will work for you.

Blood draws:
Blood draws may cause pain and bruising at the site of the blood draw. The total amount of blood drawn on the day 1 study visits is about 4 to 5 tablespoons. The pharmacokinetic studies will require a total of about 6 tablespoons of blood. Each tube of blood is slightly more than 1 teaspoon.

There may be some inconveniences encountered associated with the outpatient visits such as parking, waiting in the laboratory, x-ray department or waiting to see the doctor. Please see the protocol schedule for an approximate outline of required visits and tests.

How long will I be on the study?
You may stay on the study so long as your tumor does not progress (grow in size or spread to new locations) and you do not experience any unacceptable side effects that would require your coming off the study for your own safety. Your participation is voluntary, so you may stop treatment at any time, but we ask that you speak to your study doctor if you are thinking about this before you stop taking the medications, so they can be safely stopped.

What happens when I have finished this study?
You will be followed for any side effects that may have occurred because of the study drugs. Once these toxicities have resolved you will be returned to the care of your primary oncologist. The study team can discuss other protocol options that may be available for you at that time.

How many people will take part in the study?
Up to 30 people will take part in this Phase I study. The exact number of subjects depends upon the side effects we observe. If we see no side effects at our lower doses, then we may continue to enroll new subjects at higher dose levels. We have 5 dose levels. A minimum of 3 and a maximum of 6 people can be enrolled at each dose level.

Are there benefits to taking part in the study?
Though both drugs used in this study are Food and Drug Administration approved, the combination is experimental and has not been studied before in humans. Nine percent of people with lung cancer that has recurred after chemotherapy will respond to pemetrexed. Our theory is that sirolimus taken in along with pemetrexed may make the pemetrexed more effective but it is not possible to predict whether this will actually occur at the doses you receive or at any of the dose levels. You may receive no benefit from this drug combination, your tumors could shrink as a result of this experimental regimen, or they may simply remain unchanged. Your participation in this trial may help other people with cancer. However, as a result of participating in this investigational treatment program, you will receive evaluation and treatment of your lung cancer. All medications required by the protocol, tests required by the protocol, hospitalizations at the NIH, and physician services you receive at the NIH will be free of charge to you. As information is gathered from this trial, results will be shared with you.

What other choices do I have if I do not take part in this study?
If you choose not to participate in this protocol, we may offer you another protocol depending upon circumstances, or return you to your referring physician who may offer you standard treatments for your cancer. It is important to

understand that participation in this protocol does not guarantee long-term health care at the NIH. You may choose to receive palliative care which treats symptoms, such as pain, neuropathy, shortness of breath, or constipation, to name just a few. Palliative or comfort care will make you as active and comfortable as possible without treating your cancer directly.

Talk to your doctor about your choices before you decide if you will take part in this study. For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at *http://cancer.gov/clinicaltrials/understanding/insurance-coverage*. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Research Subject's Rights

Who do I call if I have questions? What if I want to quit the protocol?

You will be given a copy of this consent for your records. Participation in this investigational treatment protocol is entirely voluntary, and you may withdraw your consent to participate at any time without losing any benefits to which you are entitled. If complications arise from your participation in this study, efforts will be made to provide and/or arrange for medically appropriate care but we cannot guarantee that NIH will pay for all costs for that treatment or its complications. NIH also may not reimburse you for any costs incurred for tests or treatment that you receive outside the Clinical Center, including charges for laboratory tests that are required for the study or treatment for adverse effects that may have resulted from the study treatment. You are encouraged to call members of the research team at the NCI if you are concerned about any side effects from the drugs. During regular business hours, Dr. Phillip Dennis (301-496-0929) is available to address your concerns. After 5 PM, please call (301-496-1211) and ask for the Oncology fellow "on call". As a final point, please feel free to contact the NIH Clinical Center Patient Representative at 301-496-2626 if you have any questions regarding your rights under this protocol. This individual is not directly involved in this study.

What happens to my stored blood?

Some of your blood is collected and stored for possible future scientific study that may help answer lung cancer related questions. These samples will be stored in such a way that should we need to, we can identify which patient they came from so that we can correlate other clinical (routine blood work and physical exam) and laboratory (research or experimental) data. It is impossible to predict what sorts of studies may be performed on your blood, but if genetic or familial markers are to be studied, the investigators will have to obtain permission from the institutional review board (IRB) and from you if you are alive. Alternatively, you may request that your blood be discarded.

Are there any circumstances that might require my withdrawal from the study against my wishes?

* If a health condition arises that makes your continued participation dangerous to you
* If we learn something about potential dangers from other patients or other investigators
* If a regulatory agency (such as the FDA) decides the study must be discontinued
* If you are not compliant with the study medications or visits
* If the investigators decide that for any additional unanticipated reason it is unwise for you to continue in the study
* If the study is closed early for any reason

Additional research studies

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say 'no' to taking part in any of these additional studies.

Things to Think About
If you decide now that your tissue 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 tissue. Then any tissue that remains will no longer be used for research.

In the future, people who do research may need to know more about your health. While the NCI may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Your tissue will be used only for research and will not be sold. The research done with your tissue may help new developments take place in cancer treatment.

Blood and tissue samples collected from you may be stored and used in the future to study scientific questions related to this protocol. If there are any risks to you or your family associated with these scientific studies which are not covered in this consent form, your consent will be obtained before such studies are performed.

Benefits
The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks
The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making My Choice
Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our patient representative at (301) 496-2626.
No matter what you decide to do, it will not affect your care. Please check "yes" or "no" and initial.

1. My tissue may be kept for use in research to learn about, prevent, or treat cancer.

Yes	No	Initials

2. My tissue 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

3. Someone may contact me in the future to ask me to take part in more research.

Yes	No	Initials

Financial Conflict of Interest Statement:
The investigators have no financial conflicts of interest to report. This means the investigators are not receiving financial rewards for your participation in the trial.

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 other 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 study chairperson, Gideon Blumenthal, M.D., Telephone 301-796-5369 or Principal Investigator, Phil A. Dennis, M.D., Ph.D.; Telephone 301-496-0929. If you have any questions about the use of your tissue for future research studies, please contact the Clinical Director at 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 _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____