Cover Page for Standard Consent entitled: A Pilot Study of Imatinib Mesylate in Children and Adults with Sclerotic Skin Changes of Chronic Graft-Versus-Host Disease

Continuing Review Approved by the IRB on 01/10/11
Amendment Approved by the IRB on 01/19/12 Date Posted to Web: N/A
Standard

For Protocol (NCT00702689):

TITLE: A Phase II Study of Imatinib Mesylate in Children and Adults with Sclerotic Skin Changes of Chronic Graft-Versus-Host Disease

NCI # 08-C-0148 L

CTEP Protocol # 8196

INSTITUTE: National Cancer Institute

STUDY NUMBER: 08-C-0148 PRINCIPAL INVESTIGATOR: Edward W. Cowen, M.D., MHSc

STUDY TITLE: A Pilot Study of Imatinib Mesylate in Children and Adults with Sclerotic Skin Changes of Chronic Graft-Versus-Host Disease

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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. If you are signing for a minor child, "you" refers to "your child" throughout the consent document.

Your evaluation may also provide information indicating that you are eligible for other studies at the NIH. If you are found eligible for other studies, there is no obligation to participate. Before you decide to take part in this study, please take as much time as you need to ask any questions and discuss this study with family, friends, your personal doctor or any NIH health professional.

DESCRIPTION OF THE STUDY

Background

Chronic graft versus host disease (cGVHD) is a common complication of allogeneic stem cell transplant (SCT). It is the result of immune cells of the donor attacking the cells of the body of the recipient. cGVHD typically affects the skin, eyes, gastrointestinal tract (stomach and intestines), liver and lungs. Sclerotic Skin Changes (ScGVHD) is the result of fibrosis (scarring) of the skin from cGVHD. This is a serious complication of cGVHD and can lead to impairment of function, decreased quality of life and increased risk of death. This is a trial of a drug, imatinib mesylate (Gleevec™, Novartis), for children and adults with ScGVHD. Imatinib mesylate is a FDA approved drug that has been effective in the treatment of cancer in adults and children and fibrosing conditions in animals. This drug has not been used to treat GVHD so it is unknown whether it will work in this condition. As a result, this is a pilot study (explained further below) of imatinib mesylate to treat people with ScGVHD.

Purpose of the Study:

The purpose of this study is to: 1. Investigate whether imatinib mesylate results in the improvement of ScGVHD; 2. To evaluate if imatinib mesylate 200 mg daily is tolerated by patients with cGVHD 3. To assess the side effects associated with imatinib mesylate in individuals with cGVHD; 4. To establish criteria for the evaluation of ScGVHD; 5. To evaluate blood, body fluids, and tissue samples in attempt to improve our understanding of the biology of cGVHD and imatinib mesylate; 6. To assess quality of life and functional measurements in individuals with ScGVHD and to see if these change during treatment; and 7. To evaluate the response of other manifestations of cGVHD.

Study Design:

The first eight individuals enrolled on this trial were given starting doses of imatinib mesylate between 200mg and 400mg. None of these individuals were able to tolerate this dose of the drug and all required the dose to be lowered. Because of this we have redesigned the study. You will be one of approximately 10 individuals to be treated at a starting dose of 100mg of imatinib mesylate to be taken daily. You will be evaluated after one month of treatment. Depending upon the physician's evaluation of you, you may stay at the 100mg daily dose for the remainder of the study or have your dose increased to 200mg daily. Imatinib mesylate will be given as tablets to be taken orally (by mouth) once daily, every day. If you have decreased kidney function, your starting dose may be decreased to 50mg or half a tablet. Depending upon the physician's evaluation of you at your one month visit, you may continue taking the 50mg daily dose or your doctor may increase your dose to 100mg daily. You will continue to take the tablets for up to 6 months provided that your GVHD does not progress, you do not develop side effects that would require stopping the tablets, and you continue to meet the study criteria. We will ask you to record in a log (or diary) your doses of medication and the side effects you are experiencing. You will be asked to return the log to the clinical staff each time you visit the NIH Clinical Center.

During the initial 6 months of therapy you will be required to be evaluated at NIH at 1 month, 3 month and at the 6 month time point for evaluation of your cGVHD. If you continue on imatinib mesylate longer than 6 months, then you will need to be evaluated at NIH every 3 months thereafter. You will also need to be seen at your physician's office and have blood tests done to make sure you are tolerating the imatinib mesylate. See the schedule below. Patients who improve will continue to receive imatinib mesylate for up to 6 months after their best response and followed for up to 2 years. For patients who have continued response, treatment will be provided for up to two years.

Study Time Point	Frequency of Doctor Visits	Frequency of Laboratory Tests
First month you take imatinib mesylate	Doctor Visit every 2 weeks	Blood tests weekly
Month 2-6 you take imatinib mesylate	Doctor Visit once a month	Blood tests every other week
After 6 months and until you stop imatinib mesylate	Doctor Visit once a month	Blood tests once a month

The maximum duration of your involvement on this trial will be up to 1 year after stopping the study medication.

Whenever possible, drugs that you may be taking for other reasons that may interact with imatinib mesylate will be discontinued. Drugs that must be stopped 2 weeks before starting imatinib and while you are taking imatinib are:

Alfuzosin, Uroxatral®
Aprepitant, Emend®
Carbamazepine, Tegretol®, Tegretol XR® , Equetro®, Carbatrol®
Clarithromycin, Biaxin®
Eletriptan, Relpax®
Erythromycin, E-Mycin®, Eryc®, Ery-Tab®, PCE®, Pediazole®, Ilosone®
Pimozide, Orap®
St John's Wort
Warfarin, Coumadin®

While you are taking imatinib mesylate, it is important that you contact the study investigators before beginning any new prescription medicine, over-the-counter drug, supplement and/or herbal medicine as they may affect drug metabolism and cause dangerous interactions with imatinib mesylate. You will be given a list of medications and supplements to avoid when taking imatinib mesylate during the study.

Evaluations:
Prior to starting therapy, you will meet with members of the cGVHD Team, who will review your present and past medical history and determine whether you have cGVHD and ScGVHD. At a minimum, this study will require the collection of blood specimens and clinical data, which we will describe further in this consent. The purpose of this baseline visit is to perform all clinical evaluations of your cGVHD and evaluate your eligibility for this trial.

You will then continue to have regular visits at the NIH (described below) while you remain on study. Examinations can include the following:

History and Physical Examination: A summary of your medical record will be requested from your physician when you are initially referred to the NIH. In addition we will review your medical history with you and you will have a detailed physical examination. If you have had prior biopsies done, we may also ask your permission to have these sent for further evaluation at the NIH.

Blood Tests: During your screening visits, blood will be drawn from a vein in your arm. About 2 tablespoons will be used for measurements of your blood counts, liver and kidney function, serum chemistries, tests for blood clotting, screening for viruses and other routine tests. Also, approximately every 3 months, additional blood will be drawn for research purposes to study the biology of GVHD and the effects of the study medications.

HIV Testing:
As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will (not/still) be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report newly diagnosed HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.

Urine Test: Includes pregnancy test for adult females.

Pulmonary Function Test: Pulmonary Function Tests or PFTs measure the volume of air that a person can move into and out of the lungs in order to measure lung function. You will breathe into a machine that measures the air flow**.** Pediatric patients unable to perform pulmonary function testing at the NIH (typically < 8 years of age) and who require pediatric pulmonary function tests to be performed at the Children's National Medical Center will have their insurance company billed for this procedure. Those patients without insurance or for those costs incurred above insurance coverage, fees will be paid for by NIH resources up to a maximum of $5,000 per year.

Biopsy of the skin: All patients with cGVHD of the skin must have a biopsy to confirm this diagnosis. If a biopsy has not been previously obtained, then a skin biopsy at the NIH will be performed. The biopsy will be used to confirm your diagnosis and if possible, a portion of the biopsy specimen obtained will be used for research studies evaluating certain proteins that may be present in the skin. If a biopsy has been previously obtained, then a skin biopsy at the NIH is optional and will be obtained for research purposes only. A skin biopsy for research will be limited to adults 18 years of age and older. If a decision is made to perform a biopsy, the full procedure, medical reasons for doing it and all its risks and benefits will be explained to you by the treating physician who will perform the biopsy.

MRI Scan:
A magnetic resonance image (MRI) produces multiple pictures of inside the body using a strong magnetic field and radio waves to demonstrate structural and chemical changes in tissue.

CT Scan:
A computerized tomography or CT scan uses x-rays to provide multiple pictures of inside the body. The CT scan may require the injection of dye (contrast) through a needle placed in your arm. CT scans can also be done with oral contrast. The scan takes between 5 and 10 minutes to complete.

Specialty Consultations: You will also be evaluated by different specialists. Their evaluations will be used in evaluating the symptoms of your cGVHD and if there is response to therapy. The specialty consultations are:

Physical Therapist or Physiatrist plus Occupational Therapist (Rehabilitation)
Ophthalmologist (Eye Specialist)
Dentist
Dermatologist (Skin Specialist)
All necessary consultants and specialists will be provided by the NIH Clinical Center. For pediatric patients care will be provided by the NCI Pediatric Oncology Branch team and NIH Clinical Center specialists. In circumstances where additional pediatric expertise is needed, it will be provided at the Children's National Medical Center. In particular, young children will be seen by a Pediatric Pulmonologist (lung specialist) and have PFTs performed at that center.

Electrocardiogram (EKG, ECG):
A recording of the normal electrical activity of your heart is taken by placing electrodes (pieces of metal attached to wires) on the skin of your chest, arms, and legs. There is no discomfort and there are no risks.

Echocardiogram: Echocardiogram is a test that uses sound waves to create a moving picture of the heart. There is no discomfort and there are no risks.

Muga Scan:
A MUGA nuclear scan is a noninvasive diagnostic test used to evaluate the pumping function of the ventricles (lower chambers of the heart). During the test, a small amount of radioactive tracer is injected into a vein. A special camera, called a gamma camera, detects the radiation released by the tracer to produce computer-generated movie images of the heart. The MUGA scan is a highly accurate test used to determine the heart's pumping function. This test will be done at the discretion of your doctor.

Questionnaires:
We also want to know about the effect that your illness has on behavior and everyday activities. These questionnaires are called the Quality of Life (QOL) Assessments. It will take about 60 minutes to complete QOL assessment questions. These questionnaires will be performed at the time you enroll on study and then every 3 months until the completion of your enrollment on study.

Occupational Therapy Testing:
The following testing is done with the occupational therapist and will take approximately 2 hours and 10 minutes to complete. You have the right to decline participation with any of the following activities:

36 item Manual ability measure (MAM-36)-A self report which elicits the patient responses about the ease or difficulty in performing 36 common, everyday self care and household tasks. Takes 5 minutes to complete.

Jebsen Hand Function Test: Patient -completed, staff-timed test involving 7 major hand activities tasks such as feeding, writing, turning pages, stacking checkers, picking up small objects, picking up large tin cans and heavier tin cans. Both hands are tested. Takes 30 minutes to complete.

Disabilities of the Arm, Shoulder and Hand (DASH): The Disabilities of the Arm, Shoulder and Hand (DASH) Outcome Measure is a 30-item, self-report questionnaire designed to measure physical function and symptoms in patients with any of several musculoskeletal disorders of the upper limb. Takes 5 minutes to complete.

Grooved Pegboard: The Grooved Pegboard is a manipulative dexterity test consisting of 25 holes with randomly positioned slots. Pegs are placed into the respective holes in a timed test of manual dexterity. Takes 10 minutes to complete.

Assessment of Motor and Process Skills: This is an observational assessment that is used to measure the quality of a person's activities of daily living (ADL). The person will be asked to perform 2 tasks that he/she typically performs or has done in the course of their everyday life skills. Such tasks may include a household or personal care task. Takes 1 hour to complete.

SF-36: Self reported questionnaire with 36 items to evaluate eight domains of physical and mental health. Takes 10 minutes.

Human Activity Profile (HAP): A self-report measure of energy expenditure or physical fitness. The HAP consists of 94 common daily activities listed in ascending order according to the energy required to perform them. A wide variety of activities is represented, including self-care tasks, personal/household work, entertainment/social activities, and independent exercise pursuits. Takes 10 minutes to complete.

Apheresis:

You may be asked to allow us to collect some of your white blood cells. This is optional and would be done by an apheresis procedure, a common method used to collect cells from the blood. The collected cells would be used for research purposes to evaluate immune cells in your blood. Apheresis is conducted on a machine that can separate blood. In patients with central access, apheresis may be performed from the central access site; for patients who do not have central access, two peripheral lines will be used. Your blood is circulated through the apheresis machine. Some white blood cells are collected and the rest of your blood is returned back into your body along with a small amount of salt solution (saline) and blood thinning medication (anticoagulant). Blood thinning medications, heparin and/or citrate anticoagulant, are used to keep your blood from clotting during the procedure. The apheresis procedure usually takes approximately 1 hour to complete.

Potential Benefits of Participation:

The potential benefit of this treatment is that it might improve or slow the progression of your ScGVHD. Treatment may cause improvement in your GVHD and may lead to a reduction in related symptoms. However, that cannot be guaranteed and there may be no benefit to you. Your participation in this study will also allow us to learn more about cGVHD.

RISKS OR DISCOMFORTS OF MEDICATIONS:

Imatinib Mesylate: You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Many side effects go away soon after you stop taking Imatinib. In some cases, side effects can be serious, or long lasting.

Likely:

Lack of enough red blood cells (anemia)
Belly pain
Diarrhea
Nausea or the urge to vomit
Vomiting
Swelling of the arms and/or legs
Fatigue or tiredness
Decreased number of a type of white blood cell (neutrophil/granulocyte)
Decrease in the total number of white blood cells (leukocytes)
Muscle pain
Skin rash with the presence of macules (flat discolored area) and papules (raised bump)

Less Likely:

Fluid in the sac around the heart
Irritation or sores in the lining of the anus
Fluid collection in the abdomen
Constipation
Heartburn
Excess passing of gas

Bleeding in some organ(s) of the digestive tract
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
Chills
Swelling of the face
Fever
Swelling of parts of the body that are visible
Infection
Increased blood level of a liver enzyme (ALT/SGPT)
Increased blood level of a liver or bone enzyme (alkaline phosphatase)
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)
Decreased number of a type of white blood cell (lymphocyte)
Decreased number of a type of blood cell that helps to clot blood (platelet)
Weight gain
Loss of appetite
Dehydration (when your body does not have as much water and fluid as it should)
Decreased blood level of potassium
Decreased blood level of sodium
Decreased blood level of phosphate
Joint pain
Inflammation (swelling and redness) in a joint (arthritis)
Muscle cramps
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)
Headache or head pain
Cough
Shortness of breath
Irritation or sores in the lining of the voice box
Irritation or sores in the lining of the throat
Build up of a large amount of fluid between the layers of tissue that line the lungs and chest cavity
Pain in the lining of the chest cavity and/or lungs
Irritation or sores in the lining of the windpipe
Hair loss
Severe reaction of the skin and gut lining that may include rash and shedding or death of tissue
Excess sweating
Itching
Darkening of the skin
Lightening of the skin
Bleeding in the tumor site
Bleeding with a decreased number of blood cells that help to clot blood (platelets)

Rare but Serious:

Decrease in heart's ability to pump blood during the "active" phase of the heartbeat (systole)

We will carefully check you to detect any of these side effects. You are asked to report any side effects immediately because some of the side effects may be permanent. It is of utmost importance that you notify us as soon as possible if you experience any type of side effect so that you can be carefully examined before any more imatinib is given.

Although unexpected in this study, all precautions will be taken to prevent these side effects and you will be treated promptly should they occur.

Pregnancy testing and contraception

Because the use of imatinib mesylate may pose a risk to the developing fetus, women of childbearing potential (not surgically sterile or post-menopausal) must have a negative pregnancy test within 24 hours of beginning treatment with the study. Female patients must be willing to practice birth control (including abstinence) during and for 6 months after treatment, if of childbearing potential. Because the effect of imatinib on offspring of males taking imatinib is not known, birth control measures during and for 6 months after treatment should be used to prevent pregnancy of female partners of male patients taking imatinib. Effective forms of birth control include:

- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- partner's vasectomy

Optional Studies

We would like to keep some of the tissue, blood, and imaging studies that are collected for future research. These specimens and studies will be identified by a number and not your name. The use of your specimens and studies will be for research purposes only and will not benefit you. It is also possible that the stored specimens and studies may never be used. Results of research done on your specimens and studies 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 your tissue, blood, and imaging studies 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, blood, and imaging studies. Then any tissue, blood, and imaging studies that remain will be destroyed.

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. My tissue, blood, and imaging studies may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Initials_____

2. My tissue, blood, and imaging studies 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 permission to use my specimen(s) in new research not included in this consent.

Yes No Initials_____

RISKS OR DISCOMFORTS OF PROCEDURES:

Blood Draw: You may experience mild pain or bruising at the site on your arm. There is a small possibility of fainting and infection. Similarly, there is a small risk of bleeding, blockage, or inflammation (infection) of the vessel. Discomfort generally does not last long and permanent damage is extremely rare.

Skin Punch Biopsies:

- There may be minor bleeding right after the procedure and this can easily be controlled by applying pressure on the spot for a few minutes.
- Rarely, a bruise might form and this eventually goes away on its own.
- Sometimes a small infection may occur at the biopsy site. This can usually be treated with topical antibiotics.
- On the very rare occasion that a larger or deeper infection occurs, oral antibiotics may be needed for 7-10 days. An infection can be recognized by redness, soreness, and pus at the site. It generally starts 2 days or more after the procedure and does not clear up in another couple of days. These biopsy/excision sites generally heal very well, leaving red, white, dark or skin-colored flat scars.
- There may be a small scar at the site of the biopsy. When possible, biopsies will be performed on areas of the body normally covered by clothing. Sometimes, the scar that forms may be a bit thicker than usual. Rarely, a keloid (large, painful or itchy scar) may form. Keloids are more likely to form on the chin, earlobes, chest and upper backs in individuals who are Black or Asian between the ages of adolescence and 40.

Please circle and initial if you agree or disagree to having a research skin biopsy.

I agree_____ I disagree_____

Pulmonary Function Test: These tests are safe and side effects are unlikely. During the test you may be asked to breathe deeply or rapidly which may occasionally cause brief lightheadedness or slight soreness of the chest.

Eye Examination: You may experience blurry vision or sensitivity to light during and following your eye exam. These are only temporary, completely reversible and are not related to the treatment you are receiving on this study. You will be given a pair of sunglasses to protect your eyes from the light.

Imaging, Scans and Radiology Tests: (MRI and MUGA):

This research study involves minimal exposure to radiation from imaging studies performed for medical reasons. The most common discomfort is the length of time you must lay still or flat while the scan is being preformed.

- For MRI exam: Individuals with fear of confined spaces may become anxious during MRI. Individuals are at risk for injury from MRI if they have metal objects in their bodies, such as pacemakers, aneurysm clips (metal clips on the wall of a large artery), metallic prostheses, cochlear implants, or shrapnel fragments. Welders and metal workers are also at risk for eye injury because of unsuspected tiny metal fragments there.

  Please circle and initial if you agree or disagree to having a research MRI performed.

  I agree_____ I disagree_____

- For MUGA scan: Individuals may experience mild pain or bruising at the site in your arm where the dye is injected. Discomfort generally does not last long and permanent damage is extremely rare.

Risks of apheresis:

The most common side effects of apheresis are pain and bruising at the IV needle sites. Mild side-effects from the blood

thinning medication citrate are common and include chills, numbness and tingling sensations ("pins and needles") especially around the mouth, anxiety, muscle cramps, and nausea. These rapidly go away when the collection is slowed down. More serious side effects due to citrate-induced low calcium levels are uncommon and include low blood pressure, seizures, weakness, and muscle stiffness. If this happens, the apheresis procedure will be stopped, in which case these side effects quickly go away. In attempt to decrease the risk of citrate side effects, calcium and magnesium may be given through the IV during apheresis. Risks of this include changes in the heart rate and blood pressure and severe burn injury if calcium leaks out of the IV under the skin. These side effects are unlikely since calcium and magnesium would be given slowly through the large IV used for apheresis. You will be monitored closely for any side effects and the procedure will be stopped and appropriate treatment administered if necessary.

Please circle and initial if you agree or disagree to having a research leukapheresis procedure.

I agree_____ I disagree_____

Research Subject's Rights :

Your participation in this study is voluntary. You have the right to discontinue participation in this study at any time.

- You will be given a copy of this consent for your records
- You are encouraged to ask questions of the staff, your primary doctor and or family members
- There will be no charge to you for any of the cost that are directly related to this study
- You have the right to refuse any tests or procedures in this study

The pharmaceutical company that supplies the drug, imatinib mesylate, may access patient medical records on this trial.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Alternative Approaches or Treatments:

Your other choices may include:

Other treatments for cGVHD.

Taking part in another study

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 the 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.

Talk to your doctor about your choices before you decide if you will take part in this study.

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, individuals 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, Dr. Edward W. Cowen; Building 10, Room 12N238, Telephone: 301-496-4299. Other researchers you may call are: Dr. Kristin Baird, Building 10 CRC, Room 1W3750, Telephone 301-451-0391. If you have any questions about the use of your tissue for future research studies, you may also contact the Office of the Clinical Director, Telephone: 301-496-4251.

You may also call the Clinical Center Individual 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 NOVEMBER 27, 2011 THROUGH NOVEMBER 27, 2012.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____